Doctoral Thesis

Visible Light-promoted Alkyne – Alkene [2+2] Cycloaddition and Enyne Photometathesis

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Approved by

Advisor

Cheol-Min Park

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This certifies that the thesis/dissertation of Sujin Ha is approved.

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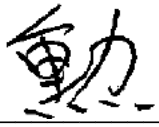

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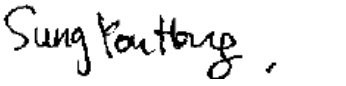

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Abstract

Cyclobutenes are good synthetic intermediates for their diversity and found in complex natural products and pharmaceuticals. Therefore, the development of synthetic method for cyclobutenes has attracted a lot of attention from the synthetic society. Because alkyne – alkene thermal [2+2] cycloaddition is a forbidden pathway, [2+2] cycloaddition of alkyne with alkene via UV activation has become an critical mean for the synthesis of cyclobutenes. While widely adopted, we were interested in exploration the complementary methods because the reaction with UV light has limited for an energy source. A variety of complementary methods for the formation of cyclobutenes using Lewis acids and transition metal catalysts have been studied. However, there is a limitation that certain functional groups are required on the substrates for activation. In a mean time, energy transfer (EnT) mechanism has been increasingly attracted attention as a substitute for visible-light photocatalysis in transformations. Here we developed [2+2] cycloaddition of alkyne with alkene through triplet energy transfer under visible light enabling the synthesis of various cyclobutenes via intermolecular reaction. Broad mechanism studies propose that the productive triplet excitation of alkenes in spite of the similar triplet energies of alkynes and alkenes can be explained by the localized spin densities on olefinic carbons. In addition, the intramolecular cycloaddition of enyne achieved the efficient synthesis for conjugated dienes through triplet tandem excitation of the formed cyclobutene products, that may provide an alternative approach to the transition metal-catalyzed ring closing enyne metathesis. 1,3-Dienes are useful intermediates in synthetic chemistry in that they can be easiely found in various transformations. Moreover, We have demonstrated the utility of our synthetic method by achieving several synthetic applications such as the synthesis for a variety of extended π-systems.

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Abbreviations

COX-2	Cyclooxygenase II
Tf	trifluoromethanesulfonate
tfacac	trifluoroacetylacetonate
TMS	trimethylsilyl
M.S.	molecular sieve
DCE	1,2-dichloroethane
cod	1,5-cyclooctadiene
THF	tetrahydrofuran
Ts	toluenesulfonyl
EWG	electro-withdrawing group
Ar	aryl
ISC	inter system crossing
THPA	3,4,5,6-tetrahydrophthalic anhydride
FEP	fluorinated ethylene propylene
UV	ultra-violet
MLCT	metal-to-ligand charge transfer
ppy	2-phenylpyridine
bpy	2,2'-bipyridine
pic	picolinic
dF	di-fluoro
dtbbpy	di-tert-butyl-2,2'-dipyridyl
Ac	acetyl/acetic

DMF	*N*,*N*-dimethylformamide
DCM	dichloromethane
WH rule	Woodward-Hoffmann rule
PC I	$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$
PC II	$Ir(dFppy)_2pic$
PC III	$Ir[dF(CF_3)ppy]_2(bpy)PF_6$
PC IV	$Ir(dFppy)_2(dtbbpy)PF_6$
PC V	$Ir(Fppy)_2(dtbbpy)PF_6$
PC VI	$Ir(ppy)_2(dtbbpy)PF_6$
n.r.	no reaction
HIV	human immunodeficiency viruses
AIDS	acquired immunodeficiency syndrome
Piv	pivalic
***m*CPBA**	*meta*-chloroperoxybenzoic acid
TEMPO	(2,2,6,6-tetramethylpiperidin-1-yl)oxyl
NMR	nuclear magnetic resonance
HRMS	high-resolution mass spectrometry
NOE	nuclear overhauser effect
TBS	tert-butyldimethylsilyl
TBAF	tetra-*n*-butylammonium fluoride
Mes	methanesulfonyl
Cy	cyclohexyl
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DFT	density functional theory

EnT	energy transfer
***p*-Tol**	*para*-tolyl
TLC	thin layer chromatography

Chapter 1.

Background of synthesis and application for cyclobutene

1.1. Cyclobutene in natural products and drugs

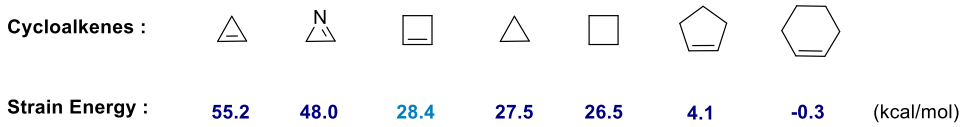


Figure 1-1. Ring strain energies of cycloalkenes

All-carbon small rings are important core structure found in many natural products and pharmaceuticals.[1] Cyclobutene has a high ring strain energy following 2*H*-azirine among small rings, and is higher than cyclopropane (Figure 1-1). Cyclobutenes with complex substituents are difficult to synthesize because they are unstable due to their intrinsic ring strain. Indeed, the synthetic approaches for cyclobutene have been rarely reported compared to other four-membered rings such as cyclobutane and cyclobutanone, which can be easily obtained photochemically and thermally. Nevertheless, the synthetic methods of cyclobutene were strongly demanded because of high utility and synthetic value of cyclobutene.

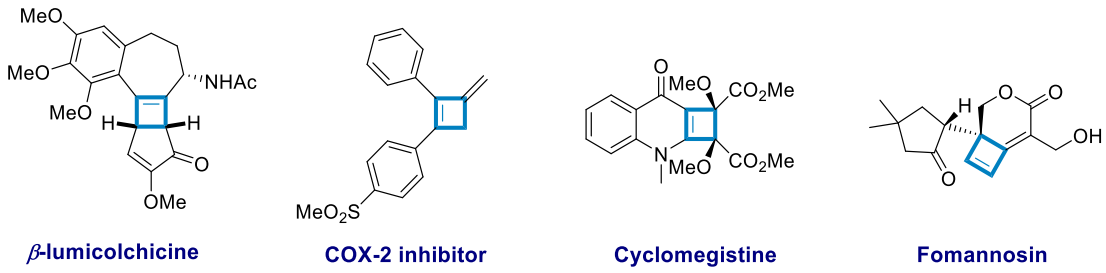


Figure 1-2. Natural and pharmaceutical products including cyclobutene

Examples of natural and pharmaceutical products with cyclobutene as its core structure are shown in Figure 1-2. *β*-Lumicolchicine is known to prevent mitosis, COX-2 inhibitor is used as anti-inflammatory analgesic drug, and cyclomegistine and fomannosin have antitumor and antiviral effects, respectively. Cyclobutene is also useful intermediate in that it can readily be transformed into other compounds due to its prominent reactivity. The conjugated 1,3-diene formed through ring opening reaction of cyclobutene by light or heat can be converted into a cyclohexene derivative after Diels-Alder reaction. In addition, the unsaturated bond of cyclobutene allows a variety of reactions, including ozonolysis, hydrogenation, epoxidation, etc (Figure 1-3).

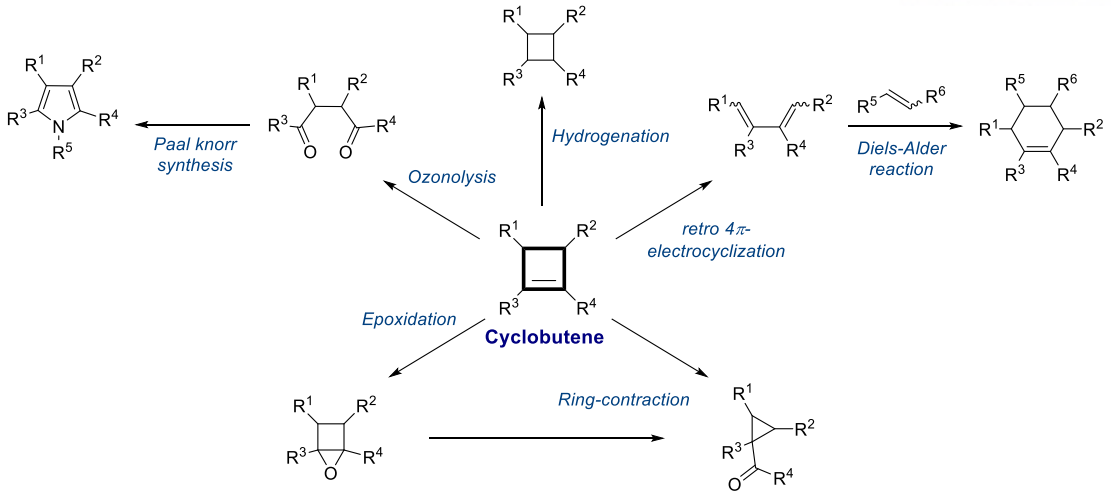


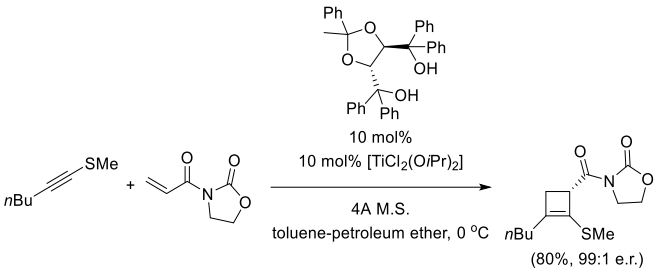
Figure 1-3. Various transformations of cyclobutene

1.2. Synthesis of cyclobutene: Alkyne – alkene [2+2] cycloadditions

Alkyne-alkene [2+2] cycloaddition is probably the most direct and effective approach to synthesize cyclobutene derivatives. According to Woodward-Hoffmann rule, the method is thermodynamically forbidden process in nature. However, the synthetic methods have been developed that are possible under certain conditions. They can be broadly classified into three categories[2]: 1) polarized [2+2] cycloaddition, 2) transition metal-catalyzed reaction, and 3) photocycloaddition.

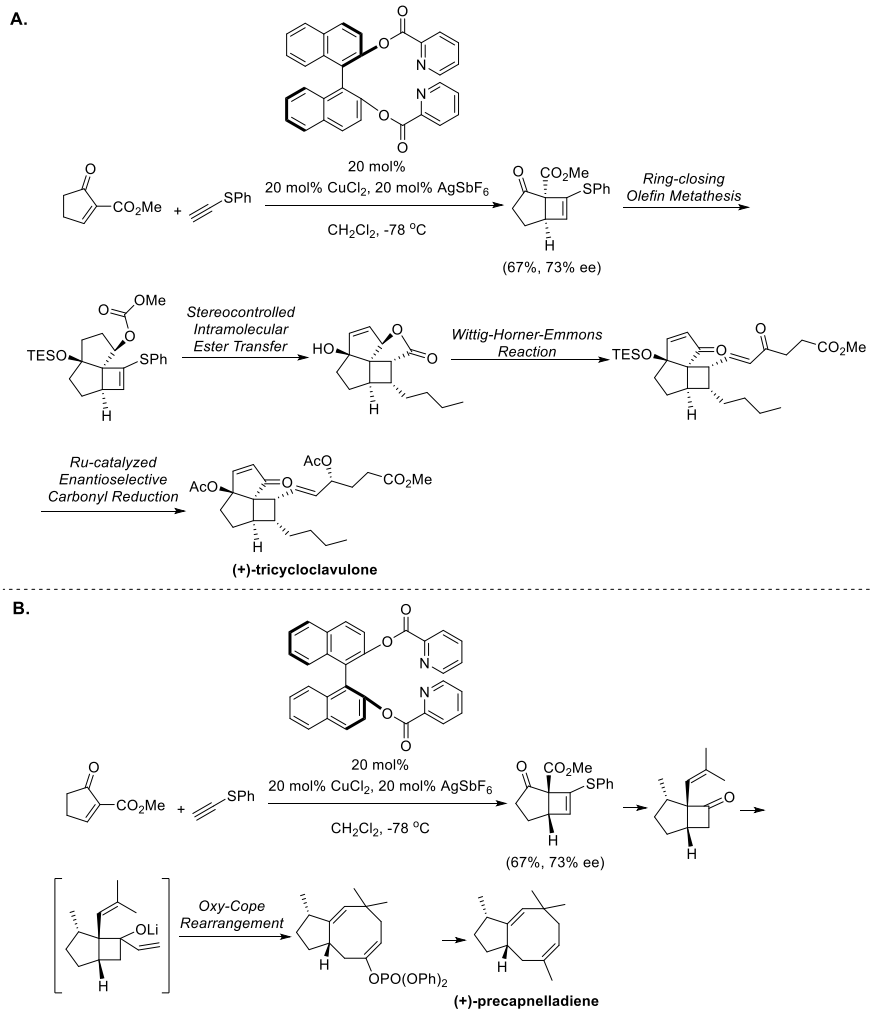
1.2.1. Polarized [2+2] cycloadditions

Polarized [2+2] cycloaddition is a reaction that occurs due to the gap between the polarities of the substrates, which should have the properties of a nucleophile and an electrophile. The significant difference in their polarity allows them exceed the activation energy barrier to form four-membered ring. In this method, Lewis acids can be employed as catalysts to activate the electrophile toward nucleophilic attack or *vice versa*. This kind of reaction is well established to achieve the higher enantioselectivity of cyclobutene. In 1989, Narasaka et al. reported the first synthetic method for catalytic enantioselective [2+2] cycloaddition, which employed alkynyl sulfide as a substrate to attain the formation of cyclobutene (Scheme 1-1).[3] In addition, alkenes containing unsaturated oxazolidinone, alkenyl and allenyl groups enable the synthesis of cyclobutane with excellent enantioselectivity. Unsubstituted, ester-substituted and unsaturated oxazolidinones are necessary to obtain high reactivity for [2+2] cycloaddition. The advantage that Lewis acid-catalyzed [2+2] cycloaddition of alkyne with alkene allows it to achieve excellent enantioselectivity of cyclobutene is useful for synthesizing natural products. Iguchi group reported the first enantioselective total synthesis of (+)-tricycloclavulone,

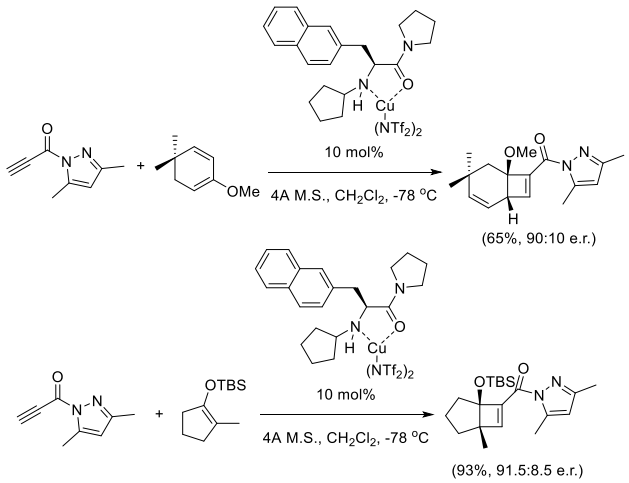


Scheme 1-1. Catalytic enantioselective [2+2] cycloaddition by Narasaka et al.

accomplishing [2+2] cycloaddition of cyclopentenone with alkynyl sulfide in 2004 (Scheme 1-2).[4] Also, they synthesized (+)-precapnelladiene with the same approach to prove the utility of the synthetic method.[5] Ishihara group achieved copper-catalyzed enantioselective cycloaddition of propiolamide with enol ether (Scheme 1-3).[6]

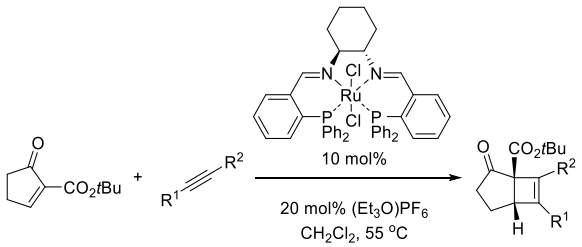


Scheme 1-2. Total synthesis of (+)-tricycloclavulone and (+)-precapnelladiene

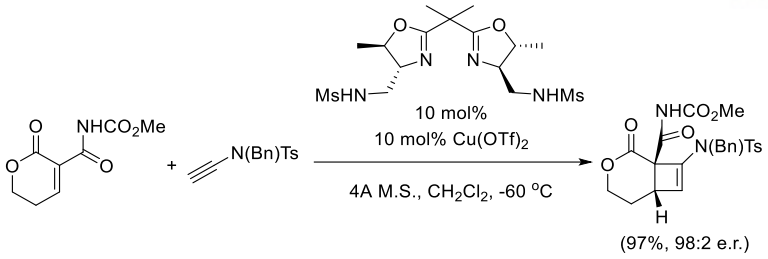


Scheme 1-3. Copper catalyzed enantioselective cycloaddition by Ishihara et al.

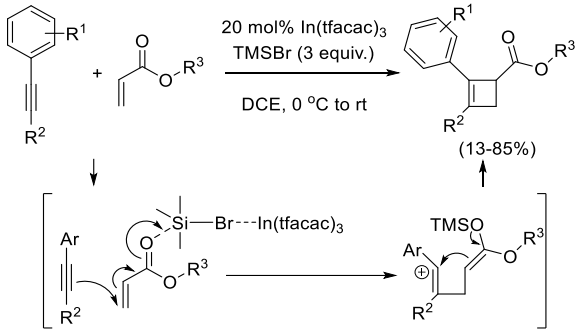
In 2011, Mezzetti et al. reported catalytic enantioselective [2+2] cycloaddition of ynamide with cyclopentenone, in other words, Ficini reaction (Scheme 1-4).[7] Ficini reaction is the stepwise [2+2] cycloaddition of ynamine with cyclic enone by heating originally. Nakada group also reported a related Ficini reaction catalyzed by the chiral ligand in combination with $Cu(OTf)_2$ as Lewis acid (Scheme 1-5).[8] In another study, a unique reactivity was elicited in the combination of $In(tfacac)_3$ with TMSBr, resulting in the [2+2] cycloaddition of aryl alkyne with acrylate (Scheme 1-6).[9]



Scheme 1-4. Modified Ficini reaction by Mezzetti et al.



Scheme 1-5. Modified Ficini reaction by Nakada et al.



Scheme 1-6. Reactivity of combined Lewis acids

1.2.2. Transition Metal Catalyzed Reactions

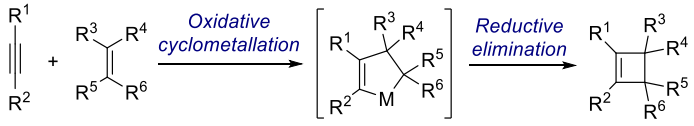
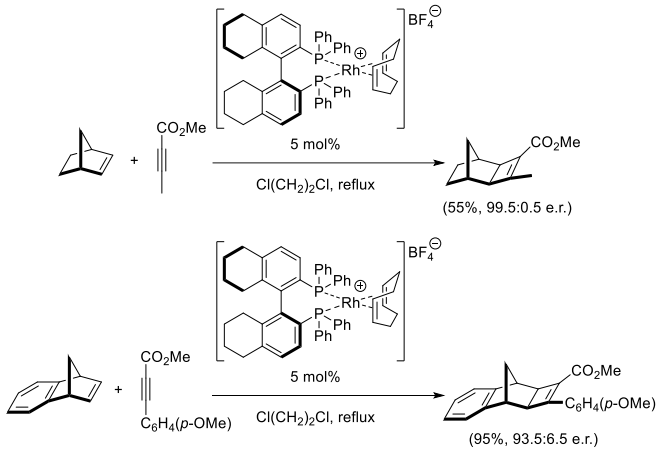


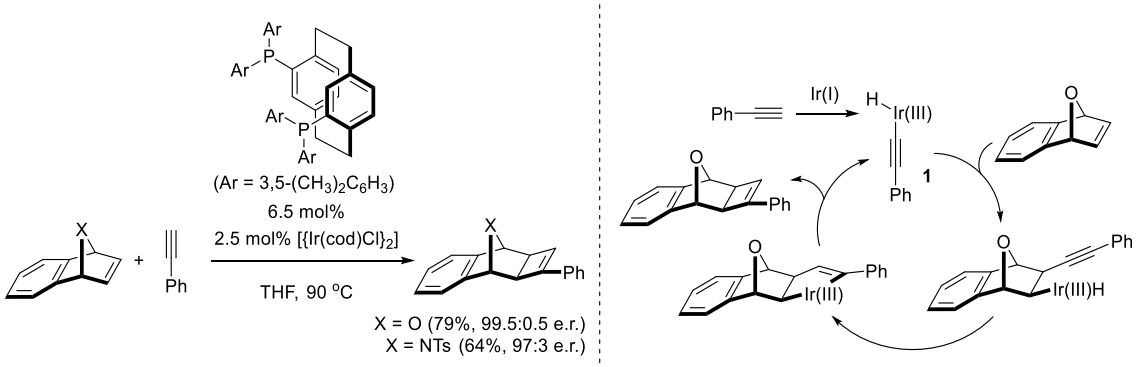
Figure 1-4. Reaction mechanism of transition metal catalyzed [2+2] cycloaddition

Many interesting reports of [2+2] cycloadditions have emerged in the field of transition metal catalyzed reactions. Mostly, the reaction mechanism is that five-membered ring intermediate was formed by oxidative cyclometallation of transition metal catalyst, and cyclobutene is produced via reductive elimination of the five-membered ring intermediate (Figure 1-4). In 2006, Shibata et al. reported enantioselective [2+2] cycloaddition of norbornene with alkynyl ester using rhodium complex (Scheme 1-7).[10] It provided good enantioselectivity and yield of cyclobutenes to synthesize tri- and tetracyclic ring.



Scheme 1-7. Rh-catalyzed enantioselective [2+2] cycloaddition by Shibata et al.

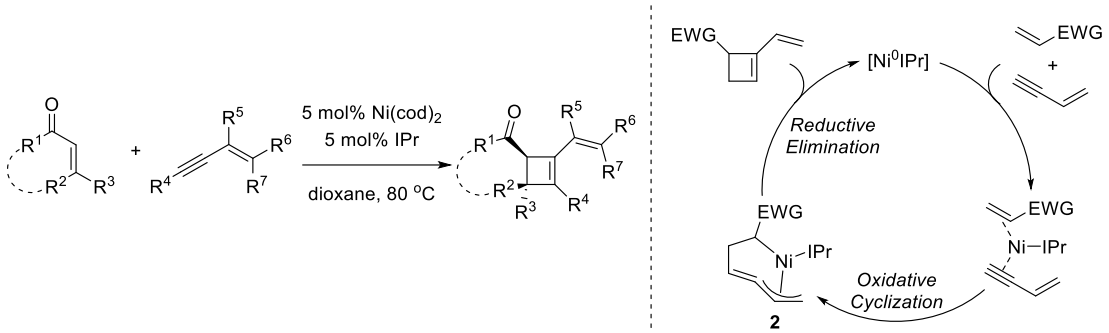
Shao group accomplished Ir-catalyzed enantioselective [2+2] cycloaddition of bicyclic alkene with terminal alkyne (Scheme 1-8).[11] Fan et al. explained the mechanism by which [hydrido(acetylene)iridium(III)] complex **1** was first formed by the oxidative addition of the Ir catalyst.[12] After migratory insertion, reinsertion and reductive elimination occurred sequentially, producing cyclobutene analogues.



Scheme 1-8. Ir-catalyzed enantioselective cycloaddition by Shao and Fan groups

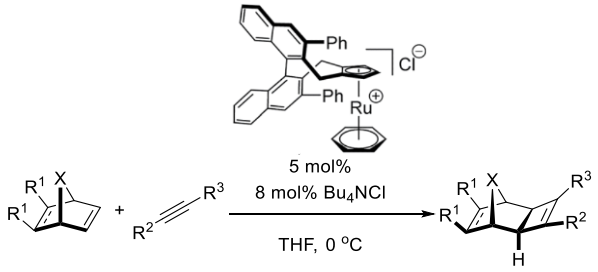
Transition metal catalyzed [2+2] cycloaddition can be achieved not only Ir but also Ni catalyst. Ogoshi group, in 2012, attained intermolecular [2+2] cycloaddition of conjugated enyne with alkene (Scheme 1-9).[13] Conjugated enyne is essential in that the Ni(0) catalyst coordinates with the conjugated enyne and alkene when oxidative cyclization occurs to produce the η^3-butadienyl nickelacycle intermediate **2**. In this moment, the regioselectivity was determined by which intermediate was thermodynamically preferred. The subsequent reductive elimination produced cyclobutene, which regenerates the Ni(0)

catalyst.



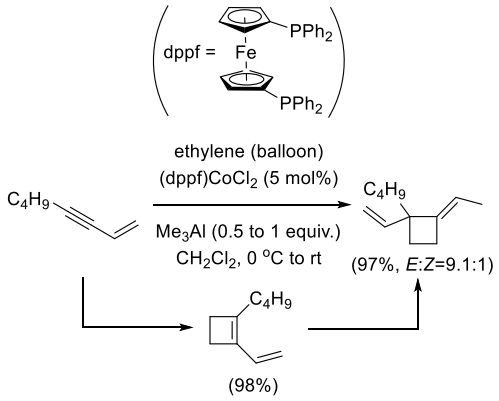
Scheme 1-9. Ni-catalyzed [2+2] cycloaddition by Ogoshi group

Cramer group reported in 2017 Ru(II) based enantioselective [2+2] cycloaddition of norbornene and alkyne with chiral ligand (Scheme 1-10).[14] It is remarkable that the reaction was previously proceeded using a cationic Ru(II) catalyst for catalysis, while a neutral Ru(II) catalyst with two open sites.



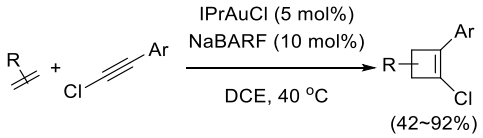
Scheme 1-10. Ru-catalyzed enantioselective cycloaddition by Cramer et al.

In 2018, RajanBabu group accomplished cobalt-catalyzed [2+2] cycloaddition to synthesize cyclobutene (Scheme 1-11).[15] In addition, they converted cyclobutene to cyclobutane through one-pot tandem [2+2] cycloaddition using a single chiral cobalt catalyst, achieving the formation of three highly selective C-C bonds. It is remarkable that inactivated ethylene and enyne were used in the reaction to obtain cyclobutene.



Scheme 1-11. Cobalt-catalyzed [2+2] cycloaddition by RajanBabu et al.

Gold catalysts are also one of the useful transition metal catalysts for [2+2] cycloaddition. Sawamura group synthesized cyclobutenes fused with macrocycles via the intramolecular [2+2] cycloaddition of alkyne with alkene (Scheme 1-12).[16] Although ring closing enyne metathesis can easily occur in transition metal catalyzed intramolecular reaction of enyne, it's impressive that this method converts enyne to intact cyclobutene quite selectively. In another example of a reaction with gold, Liming Zhang et al. reported the [2+2] cycloaddition of alkynyl chloride with inactivated alkenes, which makes it possible to synthesize cyclobutene derivatives with easy access to conversion to a variety of complex compounds.[17]



Scheme 1-12. Cyclobutene synthesis with gold catalyst by Zhang et al.

1.2.3. Photochemical [2+2] Cycloadditions

[2+2] photocycloaddition has been developed for a long time and is used in a wide range of conditions from ultraviolet (UV) to visible light. In terms of the reaction mechanism, There are two main approaches known: direct absorption (excitation) of substrate using high energy ultraviolet light and energy/electron transfer using relatively low energy with photocatalyst.[18] In case of direct excitation, olefin can be excited first from ground to singlet state (S1), and then directly undergoes addition onto other olefin or alkyne in concerted fashion (Figure 1-5).

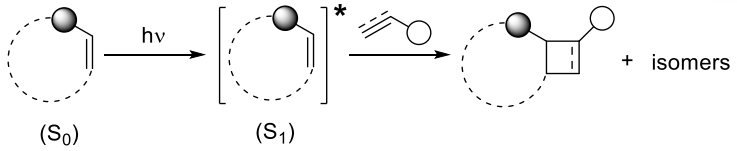
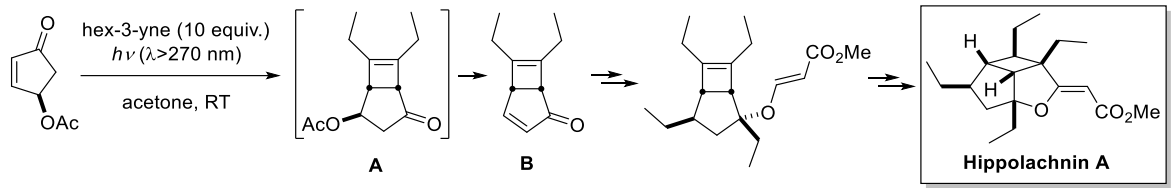


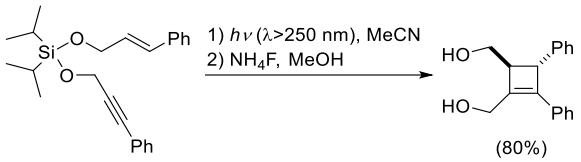
Figure 1-5. Direct excitation under uv light

In 2015, Carreira group synthesized the natural product (±)-Hippolachnin A by developing a UV light-promoted [2+2] cycloaddition (Scheme 1-13).[19]



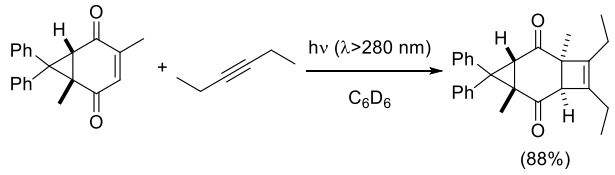
Scheme 1-13. Total synthesis of Hippolachnin A

There has been another study of intramolecular [2+2] cycloaddition using silyl-tethered enyne under UV light (Scheme 1-14).[20] They proposed a mechanism that the alkyne moiety was first converted to diradical species based on the result that the alkyl and terminal alkynes were not converted to cyclobutene instead of aryl alkyne in control experiment.



Scheme 1-14. Intramolecular [2+2] cycloaddition using silyl-tethered enyne under uv light

In 2002, Oshima group demonstrated that the [2+2] cycloaddition of homobenzoquinone derivatives can be achieved with alkenes as well as alkynes (Scheme 1-15).[21] It was inspiring that they introduced radical trapping experiments using PhSeH to explain the regioselectivity results.



Scheme 1-15. [2+2] cycloaddition of homobenzoquinone derivatives with alkynes

Recently, the studies on the [2+2] cycloaddition through energy transfer by photosensitizer have been developed enormously (Figure 1-6). Active olefins can be excited by light into a singlet state (S_1), which goes through an inter system crossing (ISC) process to become triplet state (T_1). When a photosensitizer is present, it first becomes triplet state by light, and then proceeds triplet energy transfer to the substrate.

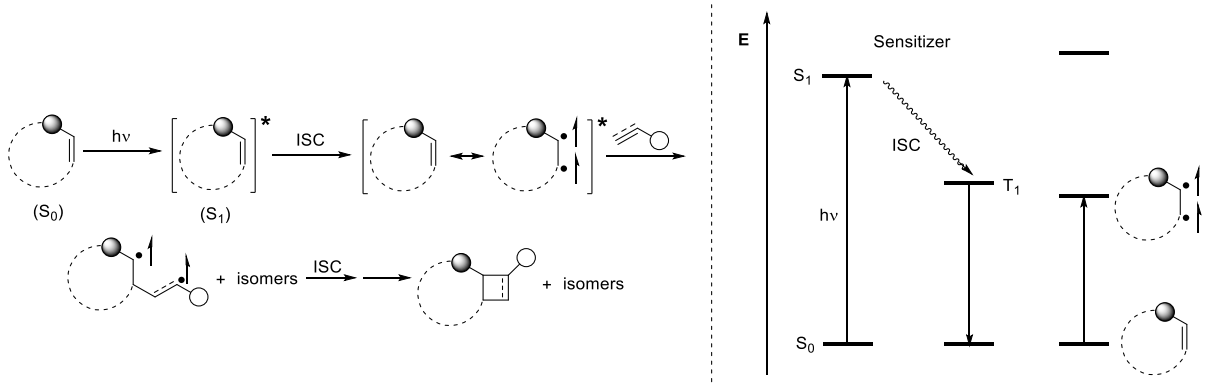
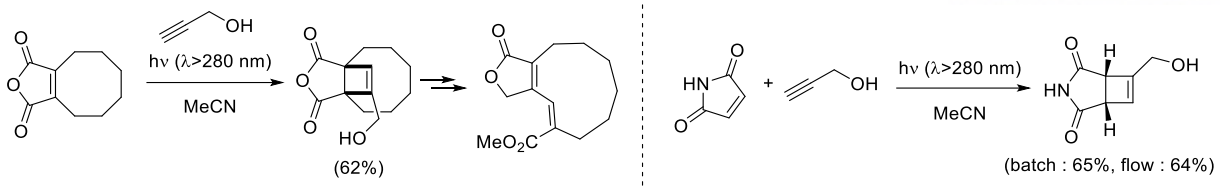


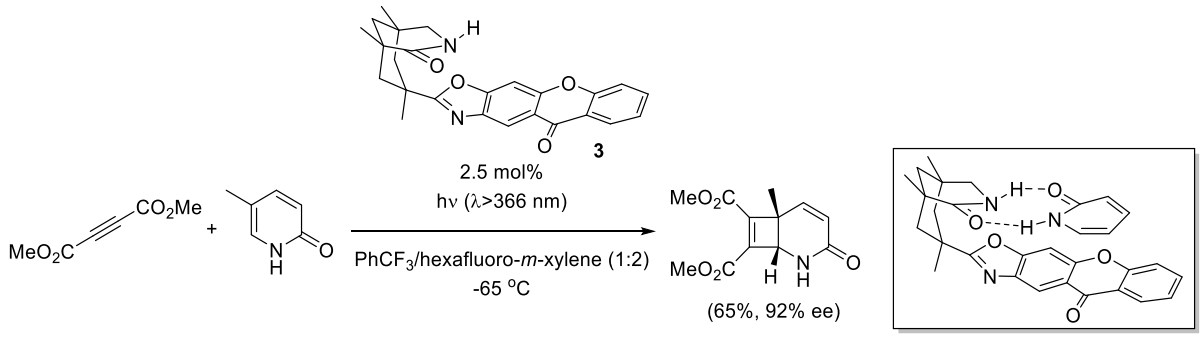
Figure 1-6. Reaction mechanism of triplet energy transfer

The triplet state of the substrate is known to have the properties of diradical species, therefore it can undergo radical addition with another olefin or alkyne to form another diradical intermediate. The intermediate transforms to cyclobutane/cyclobutene through ring-closing after ISC. Compared to the singlet state of olefins, the triplet state is useful for intermolecular [2+2] cycloaddition because it has a long lifetime up to the μs unit. The studies on triplet energy transfer through UV absorption of maleimide and anhydride have been developed in abundance. Booker Milbern group, who has continued to work in this field, reported the synthesis of cyclobutene by excitation with UV light to the triplet state of 3,4,5,6-tetrahydrophthalic anhydride (THPA) and then [2+2] cycloaddition of THPA with propargyl alcohol (Scheme 1-16).[22] In another study in the same group, they reported a method of synthesizing cyclobutene using fluoropolymer (FEP) tubes with excellent solvent resistance and UV transmission.[23] They have incorporated the method into the field of continuous chemistry to enable mass production.



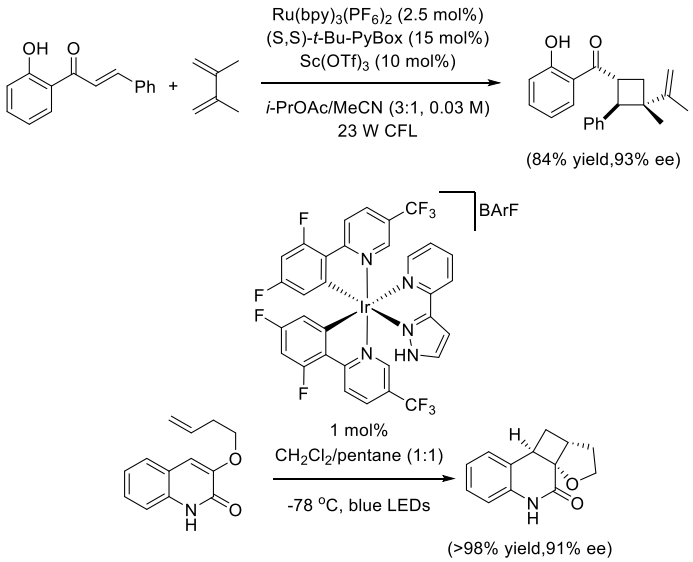
Scheme 1-16. [2+2] cycloaddition of anhydride and maleimide under uv light

Olefins can be excited to the triplet state using from UV-A (λ >360 nm) to visible (λ>400 nm) light under the influence of the process of metal ligand charge transfer (MLCT) of photocatalysts such as Ir and Ru or organic dyes as well as high energy UV light. Bach group accomplished a catalytic enantioselective [2+2] photocycloaddition using a modified xanthone **3** that can be excited by absorbing UV-A light (Scheme 1-17).[24]



Scheme 1-17. Catalytic enantioselective [2+2] cycloaddition under uv-A light

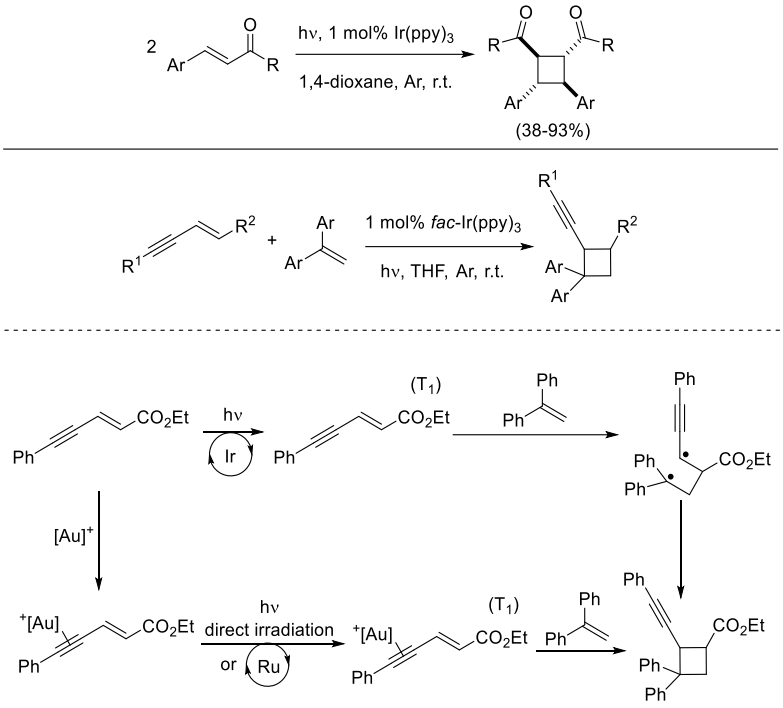
The triplet energy transfer method using a photosensitizer has the advantage of using visible light, which belongs to mild conditions, and thus has been vigorously advanced up to date. There have been many reports of visible light-promoted [2+2] cycloadditions between alkenes. In 2016, Yoon group reported that Lewis acid with chiral ligand can activate a photosensitizer electronically, which works for triplet energy transfer (Scheme 1-18).[25] They used this approach for asymmetric [2+2] cycloadditions of hydroxychalcones with Ru catalyst as a photosensitizer. They proposed mechanism that the coordination of Lewis acid significantly reduce the triplet energy level of hydroxychalcone. The same group also reported a highly effective chiral photocatalyst that recruits prochiral quinolones using a series of hydrogen-bonding and π-π interactions.[26] The association of the substrates within the chiral environment of the transition-metal photosensitizer allows expeditious stereo-induction and efficient triplet energy transfer.



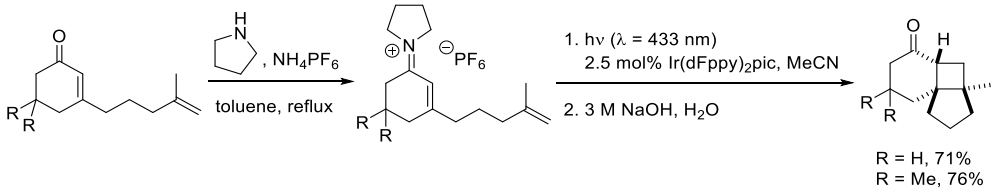
Scheme 1-18. [2+2] cycloaddition using chiral Lewis acid complex and photosensitizer

Wu group reported a general and simple method to realize the intermolecular [2+2] dimerization reaction of these acyclic olefins to construct cyclobutanes in a highly regio- and diastereoselective manner in solution under visible light (Scheme 1-19).[27] The dimerization of chalcones and cinnamic acid derivatives is one of the unique strategies to synthesize cyclobutanes, that are building blocks for a variety of bioactive molecules and natural products. In 2018, the same group reported the visible light catalytic intermolecular [2+2] photocycloaddition of alkenes with enynes to alkynyl cyclobutanes, established with good functional group tolerance and high reaction efficiency and selectivity.[28] It was found that enynes, including non-aromatics, can be sensitized by *fac*-Ir(ppy)$_3$ via an energy transfer pathway. The addition of the Lewis acid PPh_3AuNTf_2 can lead to [2+2] photocycloaddition reactions under direct visible light irradiation or sensitization by $Ru(bpy)_3(PF_6)_2$. Bach group prepared eniminium ions from the corresponding enones and enals, and found to promote to their respective triplet states by energy transfer (Scheme 1-20).[29] The photoexcited intermediates underwent intra- or intermolecular [2+2] photocycloaddition in good yields under blue LEDs. The intermolecular [2+2] photocycloaddition of an eniminium ion derived from a chiral secondary amine proceeded with high enantioselectivity. In 2018, Glorius group reported the discovery and application of dearomative cascade photocatalysis as a strategy for the synthesis of complex molecules (Scheme 1-21).[30] Visible-light-absorbing photosensitizers were used to variably form two different polycyclic molecular scaffolds through catalytic selective energy transfer by sequentially activating 1-naphthol derived arene precursor. Recently, You group achieved intramolecular dearomatization of indole derivatives by employing [2+2] cycloaddition through energy transfer under visible light (Scheme 1-22).[31] Highly

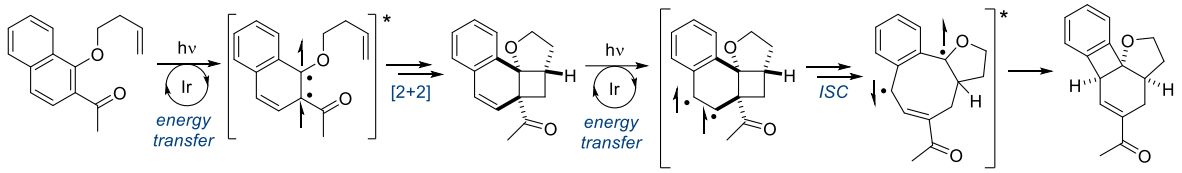
strained cyclobutene bearing tetracyclic spiroindolines, that was not normally available in thermal process, could be directly accessed with outstanding diastereoselectivity in high yield using mild process.



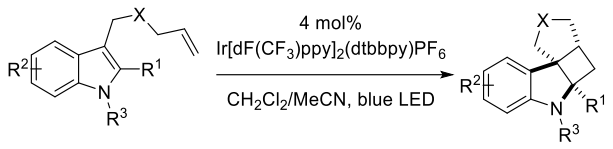
Scheme 1-19. [2+2] photocycloaddition by Wu et al.



Scheme 1-20. Enantioselective [2+2] photocycloaddition of eniminium ion

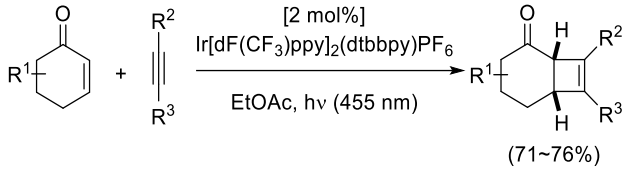


Scheme 1-21. Dearomative cascade photocatalysis by Glorius et al.



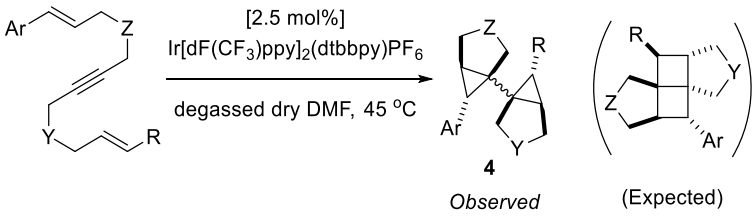
Scheme 1-22. Dearomative [2+2] cycloaddition by You et al.

However, the [2+2] cycloaddition of alkenes with alkynes in visible light is rare. Recently, there have been a few studies reported in this area. Glorius group used an iridium photocatalyst under visible light for [2+2] cycloaddition of alkene with electron-rich alkynes to form cyclobutenes (Scheme 1-23).[32]



Scheme 1-23. Alkyne-alkene [2+2] cycloaddition by Glorius et al.

Maestri group attempted the intramolecular [2+2] cycloaddition of enyne to form cyclobutene as an intermediate, which was the expected reaction to synthesize bicyclo[2.2.0]hexane derivatives through sequential [2+2] cycloaddition with alkenes (Scheme 1-24).[33] However, they obtained an unexpected molecule with two cyclopropane rings **4**, and successfully demonstrated the reaction mechanism using DFT calculations.



Scheme 1-24. Synthesis of bicyclo[2.2.0]hexane derivatives

1.3. Applications of cyclobutene : The 4π electrocyclic ring-opening of cyclobutenes

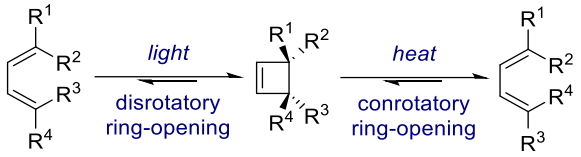
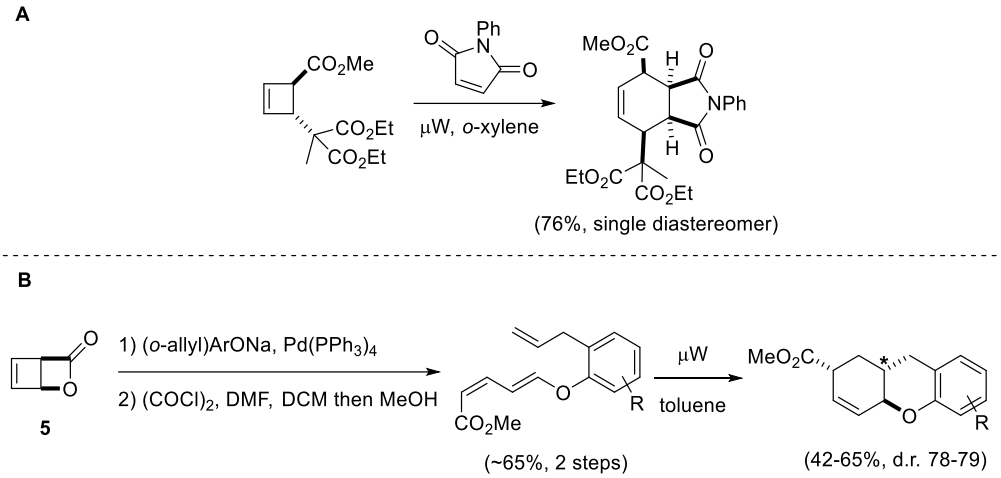


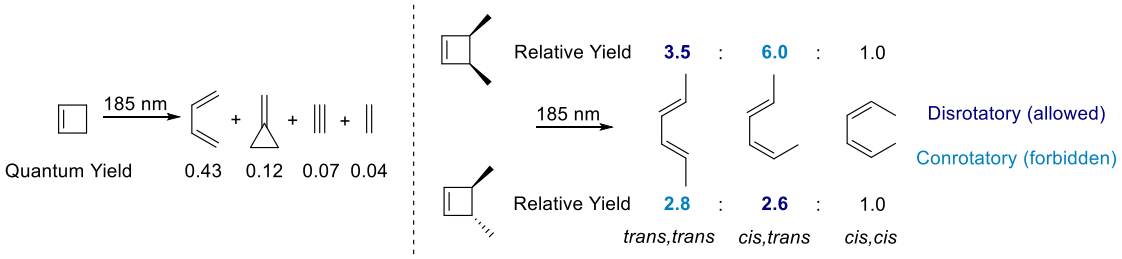
Figure 1-7. Stereoselectivity toward ring-opening of cyclobutene

Over the past 20 years, the stereoselective electrocyclic ring opening of cyclobutenes has proven to be a useful strategy for a variety of synthetic pathways.[34] The stereoselectivity toward ring-opening of cyclobutene can be controlled depending on whether it uses light or heat as an energy source. According to Woodward-Hoffmann rule (WH rule), the ring opening of cyclobutene can proceed through a conrotatory reaction mechanism by heat or a disrotatory reaction mechanism by light (Figure 1-7). The reason many chemists are eager to develop the ring-opening of cyclobutene is that it can convert cyclobutene to conjugated diene, which can be transformed into complex cyclic compounds by undergoing Diels-Alder reaction with alkenes or alkynes. There are examples for tandem reactions of ring-opening of cyclobutene and Diels-Alder reaction. Maulide group developed stereoselective domino synthesis of conjugated dienes in 2013 (Scheme 1-25).[35] They used cyclobutene ring-fused lactone **5** as a substrate, then the lactone was subjected to domino allylic alkylation and 4π electrocyclic ring opening to produce functionalized butadiene. Diels-Alder reaction proceeded between butadiene and another alkene. Photochemical ring-opening of cyclobutene has been rarely reported compared to ring-closing reaction of 1,3-butadiene because most organic substrates can absorb light with wavelengths over 230 nm. In1985, the first photochemical ring opening reaction of cyclobutene was achieved by Adam group (Scheme 1-26).[36] They observed four-photoproducts using 185 nm light in



Scheme 1-25. Tandem electrocyclic ring-opening/Diels-Alder cycloaddition

a pentane solution. Starting with Adam's work, Clark and Leigh groups developed photochemical ring-opening reaction in terms of stereochemistry. In 1987, they proved that WH rule was not always correct by obtaining conrotatory compounds, forbidden products under WH rule.[37]



Scheme 1-26. Photochemical ring-opening

Chapter 2.

Visible Light-promoted [2+2] Cycloaddition of Alkyne with Alkene

2.1. Design of synthesis for cyclobutene

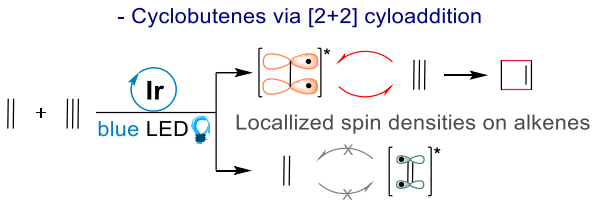


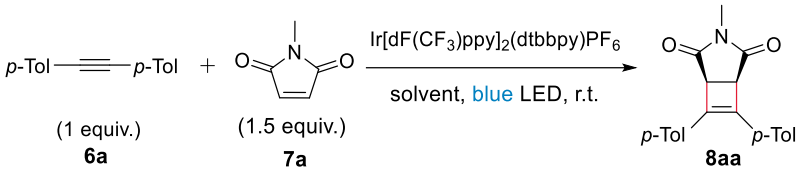
Figure 2-1. Synthesis of cyclobutene via [2+2] cycloaddition under visible light

For a long time, the [2+2] cycloaddition in visible light has been achieved only for alkenes through electron or energy transfer mechanism, and [2+2] cycloaddition of alkyne with alkene has been not clearly elucidated whether alkynes or alkenes were first activated by photocatalysts. We reported a visible light-promoted alkyne-alkene intermolecular [2+2] cycloaddition in photocatalysis to afford various cyclobutenes (Figure 2-1).[38] Extensive mechanistic studies such as triplet quenching experiment, spin density and DFT calculation make sure that the productive activation of alkenes was demonstrated by localized electron densities on unsaturated carbons of alkenes.

2.2. Reaction optimization of synthesis for cyclobutene

We started the screening with Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (**PC I**) as a photocatalyst under blue light by using diaryl alkyne **6a** and maleimide **7a** as coupling partners (Table 2-1). All yields were determined by ^{1}H NMR spectroscopic analysis against 1,1,2-trichloroethene as an internal standard. It turned out that the uses of 2.5 mol% **PC I** and nonpolar solvent (CH_2Cl_2 in 0.05 M) were optimal to afford desired cyclobutene product **8aa** in 83% yield (entry 1). The reaction underwent with somewhat lower yields under conditions of lower catalyst-loading (1 mol%) and other concentrations (0.02 M and 0.1 M; entry 2 – 4). In a change of solvents, a similar yield was shown when using chloroform instead of CH_2Cl_2 (entry 5). Changing to THF and DMF also gave lower yield, 15 and 53% respectively (entry 6 – 7). Acetone solvent, which is known as a role of photosensitizer under UV light,[39] gave 58% yield (entry 8). We performed the reaction with a mixture of acetone and water to see moisture effect (entry 9). But it didn't give any significant difference comparing to the reaction in acetone solvent. Moreover, the cycloaddition was sensitive under air, giving lower yield 48% (entry 10). It leaves the possibility of triplet-triplet energy transfer mechanism because oxygen is known as triplet quencher.[40] To ensure that the photocatalysis derives intermolecular reactions, we performed several experiments as control, however, no reaction was shown without catalyst (entry 11) or light (entry 12).

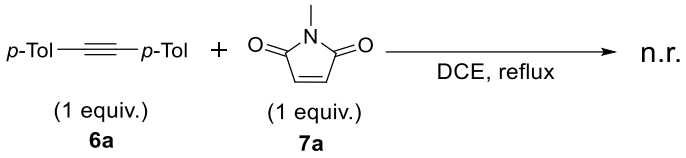
Table 2-1. Optimization of alkyne – alkene [2+2] cycloaddition[a]



Entry	Photocatalyst [mol%]	$E_{1/2}(M^*/M^+)/E_{1/2}(M^*/M^-)$ (V vs SCE)	E_T (kcal/mol)	Solvent (M)	Yield
1	PC I [2.5]	-0.89 / 1.21	60.8	CH_2Cl_2 (0.05)	83% (76%[b])
2	PC I [1]	-0.89 / 1.21	60.8	CH_2Cl_2 (0.05)	75%
3	PC I [2.5]	-0.89 / 1.21	60.8	CH_2Cl_2 (0.02)	80%
4	PC I [2.5]	-0.89 / 1.21	60.8	CH_2Cl_2 (0.1)	74%
5	PC I [2.5]	-0.89 / 1.21	60.8	$CHCl_3$ (0.1)	73%
6	PC I [2.5]	-0.89 / 1.21	60.8	THF (0.1)	15%
7	PC I [2.5]	-0.89 / 1.21	60.8	DMF (0.1)	53%
8	PC I [2.5]	-0.89 / 1.21	60.8	acetone (0.1)	58%
9[c]	PC I [2.5]	-0.89 / 1.21	60.8	acetone/H_2O (0.05)	60%
10[d]	PC I [2.5]	-0.89 / 1.21	60.8	CH_2Cl_2 (0.05)	48%
11	-	-	-	CH_2Cl_2 (0.05)	trace
12[e]	PC I [2.5]	-0.89 / 1.21	60.8	CH_2Cl_2 (0.05)	n.r.

[a] Reactions were conducted under argon atmosphere with 0.05 mmol scale. **8aa** is a racemic. n.r. = no reaction. [b] Isolated yield after 4 h. [c] acetone : H_2O = 9:1. [d] Reaction was conducted under air. [e] Reaction was conducted in the dark.

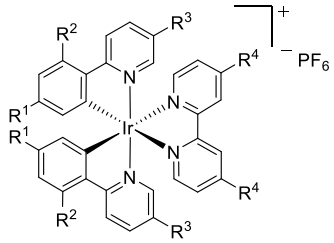
[2+2] cycloaddition of alkene with alkyne is a forbidden reaction in thermal condition, however, a few [2+2] cycloadditions of reactive alkyne with alkene have been reported.[41, 42] To make sure that the reaction is driven by photo-reaction, we performed another control experiment in thermal condition. When **6a** and **7a** heated up to reflux in 1,2-dichloroethane soluion without photocatalyst and blue LED, cyclobutene product **8aa** couldn't be formed (Scheme 2-1).

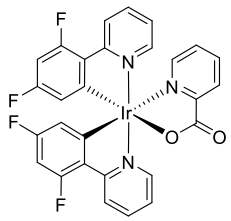


Scheme 2-1. Thermal condition of [2+2] cycloaddition of alkene with alkyne

At this moment, we examined the underlying properties allowing the reactivity of photocatalysts, such as various iridium photocatalysts (**PC I** – **PC VI**), ruthenium catalyst and organic dye (Table 2-2). To figure out which mechanism would be operative between two possible reaction processes, one is energy transfer and the other is electron transfer, we compared the triplet energy and redox potential of alkene **7a** (E_T = 55.9 kcal/mol and $E_{p/2}^{red}$ = -1.16 V vs. SCE) with those of photocatalysts. The yields of cyclobutene **8aa** have good correlation with the triplet energy levels of the photocatalysts, but their redox properties didn't appear to be related to the results of the reaction. For instance, **PC I** with the highest triplet energy proved that it is the most effective catalyst for the reaction (E_T = 60.8 kcal/mol),

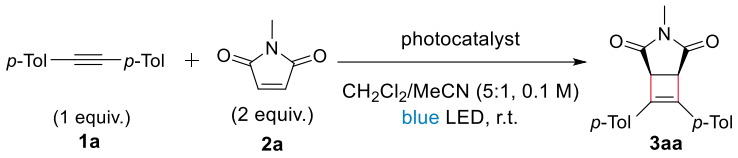
Table 2-2. Screening of catalysts for alkyne – alkene [2+2] cycloaddition[a]





PC I R^1= F, R^2= F, R^3= CF_3, R^4= ^{t}Bu
PC III R^1= F, R^2= F, R^3= CF_3, R^4 = H
PC IV R^1= F, R^2= F, R^3= H, R^4 = ^{t}Bu
PC V R^1= F, R^2= H, R^3= H, R^4 = ^{t}Bu
PC VI R^1= H, R^2= H, R^3= H, R^4 = ^{t}Bu

PC II



Entry	Photocatalyst [mol%]	$E_{1/2}(M^*/M^+)/E_{1/2}(M^*/M^-)$ (V vs SCE)	E_T (kcal/mol)	Yield
1	PC I [5]	-0.89 / 1.21	60.8	76%
2	PC II [5]	-1.23 / 1.40	60.5	74%

3	PC III [5]	-0.97 / 0.97	60.4	74%
4	PC IV [5]	-0.93 / 1.14	55.4	62%
5	PC V [5]	-1.04 / 1.07	53.0	35%
6	PC VI [5]	-0.96 / 0.66	49.2	trace
7	$Ru(bpy)_3(PF_6)_2$ [5]	-0.81 / 0.77	46.5	n.r.
8[b]	Eosin Y [5]	-1.11 / 0.83	43.6	n.r.

[a] Reactions were conducted under argon atmosphere with 0.05 mmol scale. **8aa** is a racemic. n.r. = no reaction. [b] Green LED was used, not blue one.

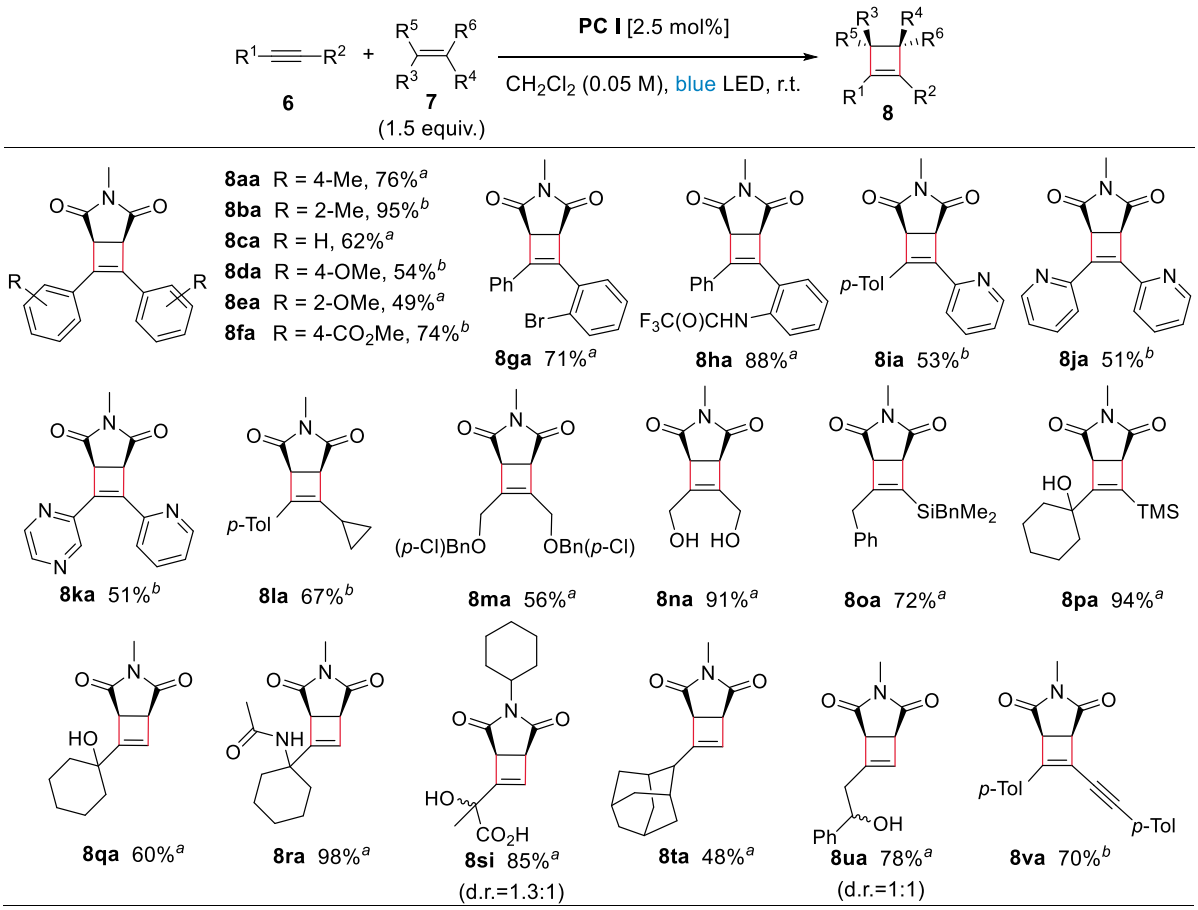
while its reduction potential is not sufficient for the reduction of maleimide **7a** ($E_{1/2}(M^*/M^+)$ = -0.89 V vs. SCE). When **PC VI** with somewhat higher reduction potential but a triplet energy much lower than that of **7a** was used ($E_{1/2}(M^*/M^+)$ = -0.96 V vs. SCE and E_T = 49.2 kcal/mol), a trace conversion was shown. In the same manner, a similar trend was shown for **6a** (E_T = 56.7 kcal/mol and $E_{p/2}^{red}$ = -2.5 V, $E_{p/2}^{ox}$ = 1.59 V vs. SCE) as well, indicating that the yields correlated well with the triplet energy levels of photocatalysts comparing to their redox potentials. These results do not clearly explain which counterpart of alkene and alkyne undergoes productive triplet excitation, but led us to suggest that the energy transfer process is working for the [2+2] cycloaddition of alkene with alkyne.

2.3. Substrate Scope for Intermolecular [2+2] Cycloaddition

The scope of intermolecular reaction was investigated with the optimized conditions. First, the steric and electronic effects were investigated by reacting substituted diarylalkynes with alkene **7a**. It turned out that all alkynes which have electron-rich or deficient were tolerated well (Table 2-3, **8aa – 8ha**). The usefulness of biologically active heterocyclic compounds motivated us to investigate alkynes substituted with pyridines and pyrazines. We were pleased with the fact that these heterocyclic alkynes reacted easily to provide desired products in good yields (**8ia – 8ka**). Moreover, the reaction of cyclopropyl arylalkyne **6l** and alkene **7a** afforded **8la** with the cyclopropyl ring intact in 67% yield.

Alkynes substituted with alkyl groups as well as the aryl substitution were investigated. We were gratified to know that the reaction of dialkylalkynes **6m** and **6n** underwent to give the desired products **8ma** and **8na**. Furthermore, both alkynes substituted silyl group and substituted free **6o** – **6u** readily worked well during the reaction. In addition, we were interested in whether the reaction could endure alkynes with carboxylic acid and free hydroxy groups, that would make precluding protection chemistry. Substrates **6s** and **6u** certainly provided cyclobutene **8si** and **8ua** in good yields. The reaction of conjugated diyne **6v** also proceeded well to provide the desired alkyne substituted cyclobutene **8va** in 70% yield.

Table 2-3. Scope of alkyne moiety for alkyne – alkene [2+2] cycloaddition

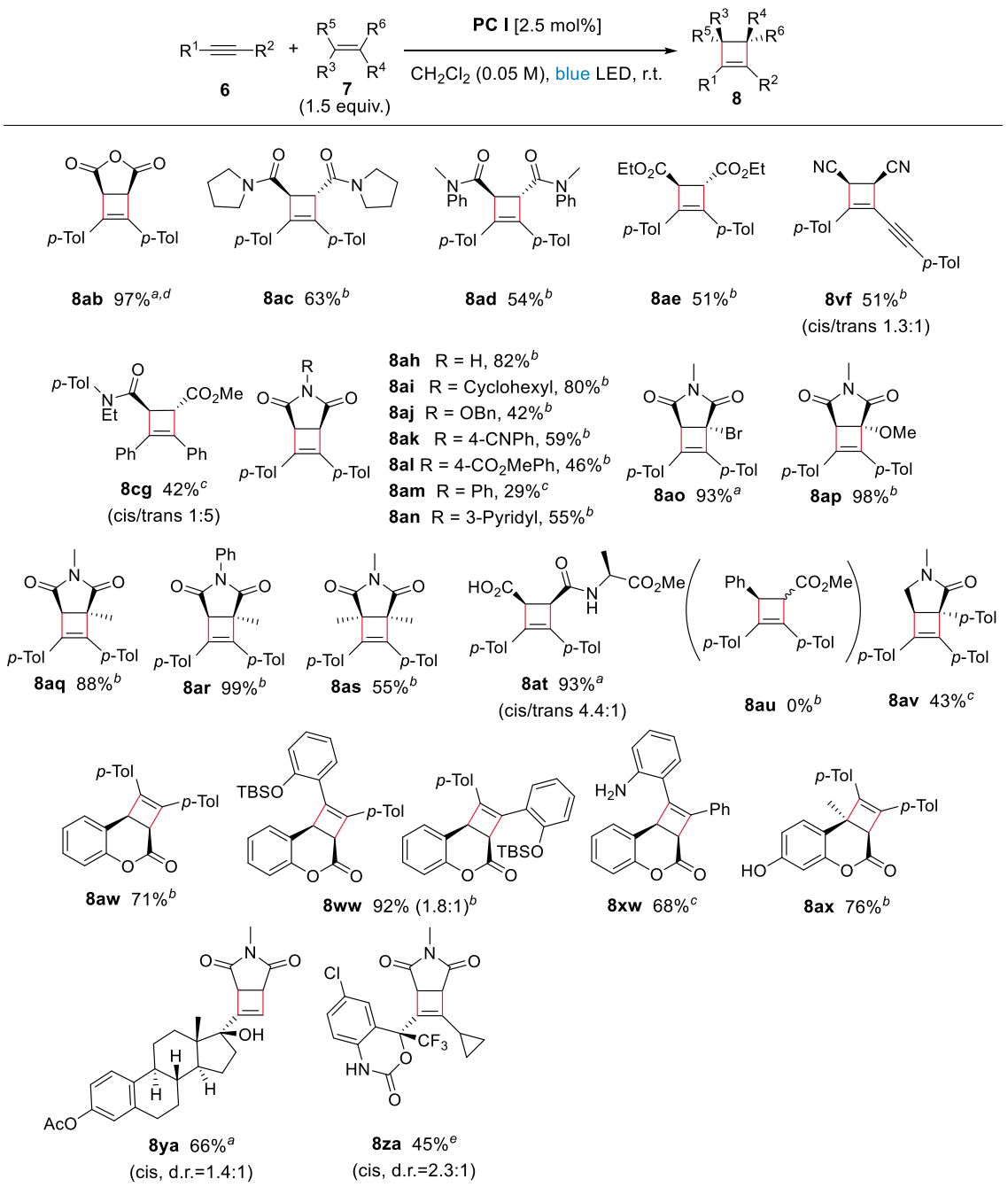


Unless other noticed, all reactions were performed under blue light using 12 W LED strip and argon gas with 0.1 mmol scale; Isolated yields; all cyclobutenes are racemic. [a] Reaction time : 1 – 18 h [b] Reaction time : 24 – 48 h

We also examined the reactivity of the alkene moiety and it was turned out that good conversion can be achieved with alkenes bearing electron withdrawing groups. Hence, those functional groups including anhydride, amide, ester, and nitrile were turned out to be efficient for the reaction (Table 2-4, **8ab** – **8cg**). A variety of N-substituted maleimides were participated in the reaction to figure out the concrete steric and electronic effects of maleimides for cycloaddition. It was found that N-H free and N-cyclohexyl maleimides **7h** and **7i** provided the desired products **8ah** and **8ai** in good yield. A variety of other N-substituents for maleimides with N-benzyloxyl, (*p*-cyano)phenyl and (*p*-methylester)phenyl groups were allowed to give cycloadducts in moderate to good yields (**8aj** – **8al**). Besides, cyclobutene containing N-heteroarene could be obtained using maleimide **7n**.

Moreover, while investigating the scope of maleimides, yields of cyclobutenes were shown in broad range depending on the N-substituent groups. Because of this, we gauged the correlation between

Table 2-4. Scope of alkene moiety for alkyne – alkene [2+2] cycloaddition



Unless other noticed, all reactions were performed under blue light using 12 W LED strip and argon gas with 0.1 mmol scale; Isolated yields; All cyclobutenes are racemic. [a] Reaction time : 1 – 18 h [b] Reaction time : 24 – 48 h [c] Reaction time : 53 h – 3 d [d] Obtained as N-benzylamide form by one-pot addition with benzylamine reagent after finishing cycloaddition; Two-step yield. [e] Reaction time : 5 d; 15 equiv of alkene was added into the reaction and **PC III** was used not **PC I**.

reaction effectiveness and electronic effect (Figure 2-2). There was a clear correlation; In general, the

lower yields were obtained from the reaction using N-aryl maleimides compared to those of N-alkyl maleimides **7i**, in that case the low electron density of the unsaturated carbons seems to be caused by electronic delocalization to the aromatic ring. On the contrary, electron deficient aryl maleimides **7k** and **7l** gave higher yields. It has also good agreement with their electronic effects.

Furthermore, we investigated the substitution influence on maleimide's olefinic part. The maleimides **7o** – **7r** substituted with halogen, methoxy and alkyl groups afforded the cycloadducts in outstanding yields. However, maleimide **7s** substituted with dimethyl group gave the corresponding cyclobutene in moderate yield apparently because of steric effect. The cycloaddition of alkene **7t** prepared using L-alanine proceeded well, affording cyclobutene **8at** in 93% yield. While acyclic mono-activated alkenes like methyl cinnamate failed to afford the desired cycloadduct (Scheme 2-2, **8au**), cyclic alkenes of mono-activation containing lactam **8av** and coumarins (**8aw** – **8xw**) gave moderate to good yields. In addition, a highly substituted cyclobutene **8ax** with a quaternary center was obtained in good yield (76%). We conjecture that the miscarriage for the reaction using acyclic mono-activated alkenes can be ascribed for quenching of catalyst due to E/Z isomerization. In the meantime, the reaction of **6a** with **7w** was compared with the reaction under UV light. We found that the reactions under both UV light 254 nm and 365 nm were sluggish giving 17% and 3% yields, respectively. (Scheme 2-3). In addition, late stage functionalization toward mercantile pharmaceuticals bearing alkyne groups underwent well when using acetyl protected 17α-ethynylestradiol and Efavirenz, resulting **8ya** and **8za** in good yields. 17α-ethynylestradiol is an estrogen medication which is used widely in birth control pills in combination with progestins. It was widely used for the treatment of menopausal symptoms, gynecological disorders, and certain hormone-senstive cancers. It is usually taken by mouth. Efavirenz is an antiretroviral medication used to treat and prevent HIV/AIDS. It may be used for prevention after a needlestick injury or other potential exposure. It is taken by mouth once a day.

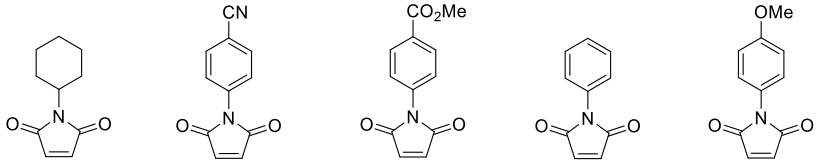
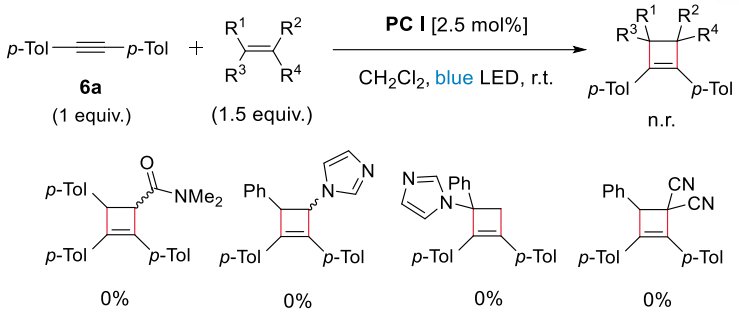
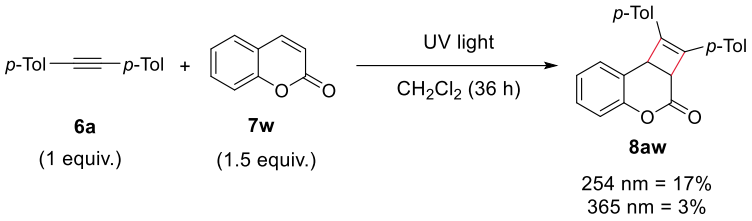


Figure 2-2. Electronic effect of N-substituted maleimides



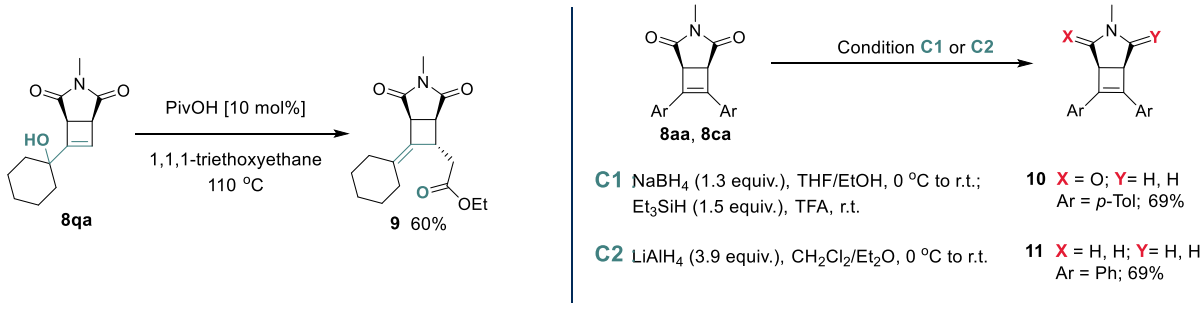
Scheme 2-2. Scope of failed alkenes



Scheme 2-3. Reactions under uv irradiation

2.4. Synthetic Applications of Cyclobutene

A variety of transformation more illustrated the synthetic application of cyclobutenes. First, we tried Johnson-Claisen rearrangement that is the reaction of an allylic alcohol with an orthoester to yield a γ, δ-unsaturated ester (Scheme 2-4). Pivalic acid was used to catalyze this reaction. Exomethylene cyclobutane **9** was successfully prepared from allylic alcohol **8qa**. This rearrangement required high temperature (110 °C) to complete. Furthermore, γ-lactam and pyrrolidine were readily prepared by the reducing cyclobutenes **8aa** and **8ca** fused succinimide moiety.



Scheme 2-4. Synthetic applications of cyclobutene

The transformation of cyclobutene can be extended when utilizing unsaturated double bond (Figure 2-3). A trial of ozonolysis gave diketone **12** with 75% yield. It can be further transformed to bicyclic compounds via Paal-Knorr synthesis, which is a reaction that generates either furans, pyrroles, or thiophenes from 1,4-diketones. The reaction of cyclobutene **8ca** with *m*-chloroperbenzoic acid (*m*CPBA) gave epoxide **13** to form three-four-five-membered tricyclic rings. It can undergo ring contraction treated by Lewis acid to afford cyclopropane ring **14** in 82% yield. The cyclobutene **8ae** synthesized from diethyl fumarate **7e** and di(*p*-tolyl)acetylene **6a** can be converted to 1,3-dienes **15** via 4π-electrocyclic ring opening under high temperature. We tried not only normal but also inverse electron-demand Diels-Alder reactions of diene with several condition, but both failed to give cyclohexene product.

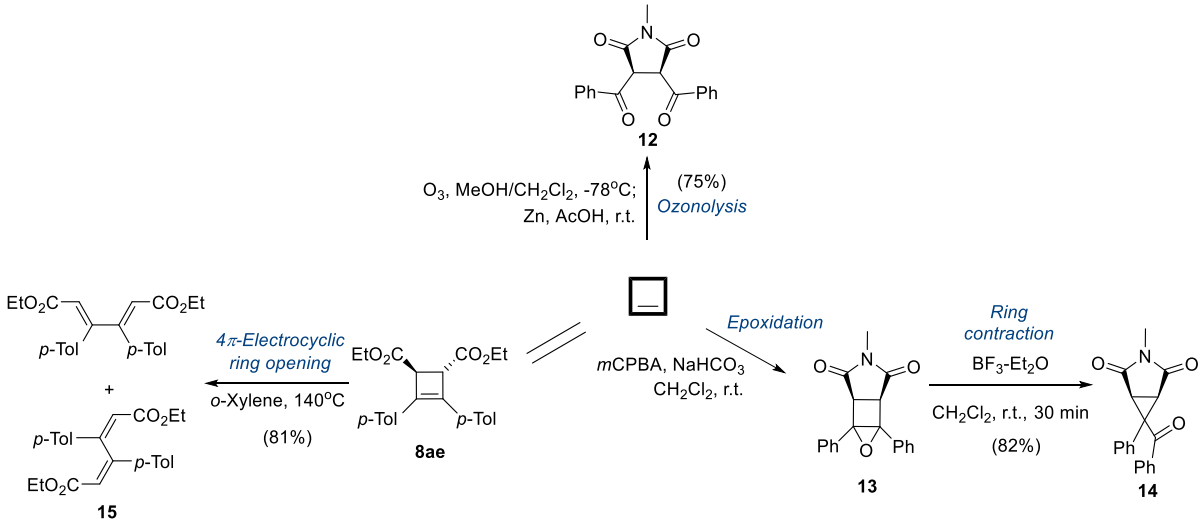


Figure 2-3. Various transformations of cyclobutene

2.5. Mechanism Study of [2+2] Cycloaddition of Alkyne with Alkene

To find out whether a radical chain process is involved in the reaction, light on-off experiments were proceeded for the intermolecular reaction (Figure 2-4). The reaction stopped without light in the experiment, that excludes a radical chain process.

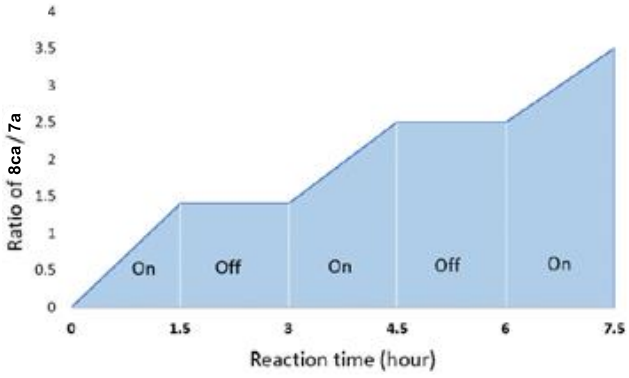
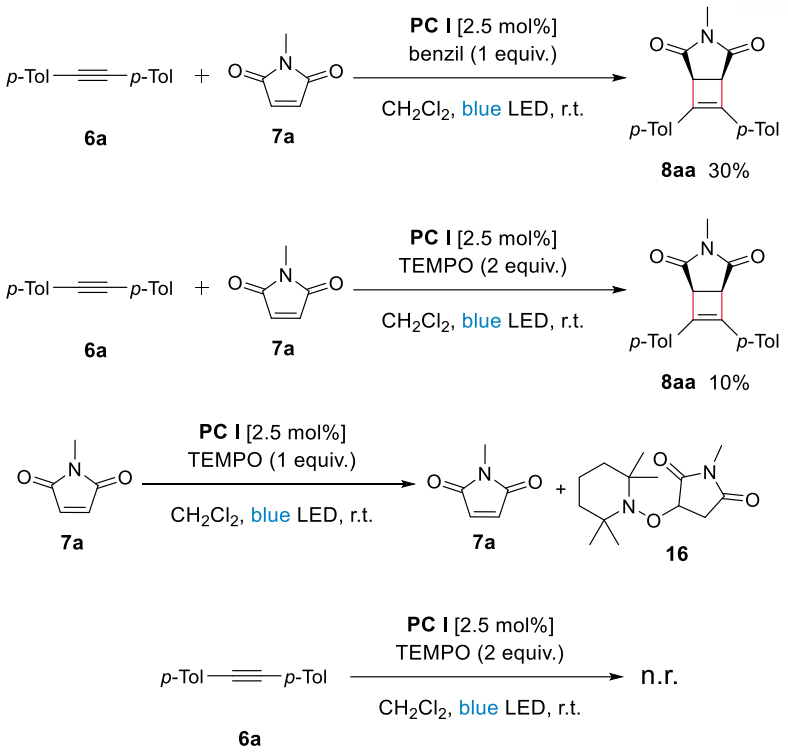


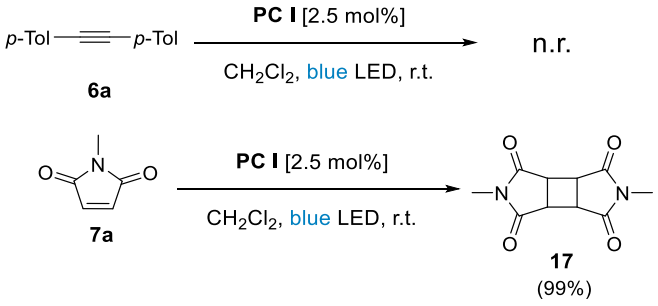
Figure 2-4. Light on-off experiments on intermolecular reaction

The measurement of quantum yield for the intermolecular cycloaddition of **6a** with **7a** was also performed. The quantum yield 0.91 supports that the reaction isn't radical chain reaction. To further corroborate that the triplet energy transfer mechanism is in operation for the reaction, the experiments using benzil (E_T = 53.4 kcal/mol) as triplet quencher were proceeded, and it was turned out that the reaction gave significantly lower yield in 30% comparing to standard reaction (Scheme 2-5). Another triplet quenching experiment with TEMPO (E_T = 52 kcal/mol) also afforded cyclobutene product in low yield. TEMPO is generally known as radical scavenger. The reaction of maleimide **7a** alone with TEMPO gave a mixture of **7a** and TEMPO attached adduct. We couldn't separated two compounds but we obtained ^{1}H NMR and MS data of the mixture. Also the reaction of di(*p*-tolyl)acetylene **6a** alone with TEMPO didn't give any expected product, only remaining alkyne **6a**. There is reported that the triplet state of alkene is diradical species. we speculated that alkene would be excited to triplet state by photocatalyst because the diradical intermediate of alkene **7a** was captured by TEMPO. However it's not certain because we couldn't obtain TEMPO attached product **16** during the alkyne – alkene [2+2] cycloaddition with TEMPO.



Scheme 2-5. Experiment of triplet quenchers

The photo-reactions without counterparts were performed to figure out which substrate is activated by photocatalyst (Scheme 2-6). While the reaction of alkyne **6a** alone didn't afford any product, N-methyl maleimide **7a** dimerized to form cyclobutane **17** when subjected to the condition. This result proposed the possibility that alkene is excited to the triplet state in photocatalysis.



Scheme 2-6. Control experiments without counterpart

We also performed Stern-Volmer quenching experiment with various photocatalysts using **6a** and **7a** as quenchers, investigating the relation of catalyst quenching with triplet energy level or with redox

property (Figure 2-5). The degree of catalyst quenching by **6a** showed nice consensus for the triplet energy levels, not the reduction and oxidation potentials, that **PC I** with the most effective triplet energy level is shown as the best photocatalyst for the reaction. The same tendency was observed for the quenching by **7a**, although the degree of catalyst quenching was less effective than that by **6a**. These results show that the reaction is promoted through triplet energy transfer.

Photocatalyst (0.1 mM)		Quencher : 1a					
Cat.	Max emission wavelength	0 mM	2 mM	4 mM	6 mM	8 mM	10 mM
PC I	472 nm	1	3.0568	4.7348	7.1689	9.5936	12.1958
PC IV	505 nm	1	1.4928	2.2200	2.6175	3.2100	3.8640
PC V	527 nm	1	1.1203	1.3385	1.4381	1.6377	1.7515
PC VI	562 nm	1	1.0115	1.0763	1.0814	1.0106	1.0279

Photocatalyst (0.1 mM)		Quencher : 2a					
Cat.	Max emission wavelength	0 mM	2 mM	4 mM	6 mM	8 mM	10 mM
PC I	472 nm	1	1.0900	1.6040	1.6821	2.0379	2.7735
PC IV	505 nm	1	1.0334	1.0874	1.2463	1.3397	1.4432
PC V	527 nm	1	0.9846	0.9468	1.1190	1.1403	1.1878
PC VI	562 nm	1	0.9530	0.8810	1.02276	0.9031	0.9291

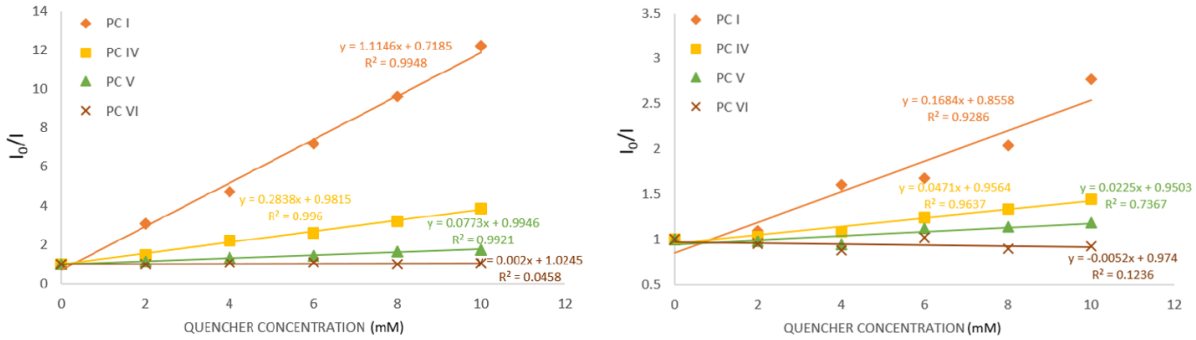


Figure 2-5. Stern-Volmer plot using 6a and 7a as quenchers

Due to the similar triplet energy levels of alkyne **6a** (56.7 kcal/mol) and **7a** (55.9 kcal/mol), It remains a question that which moieties achieves the productive triplet activation. Alkyne **6a** seems to be better one as a quencher than alkene **7a** in Stern-Volmer quenching experiment. It may propose that triplet alkynes would participate in [2+2] cycloaddition, not alkenes. On the other hand, Quenching of standard photocatalyst by alkyne **6m** was not shown Because the alkyne **6m** has higher triplet energy 74.1 kcal/mol than that of photocatalyst. However the reaction of alkyne **6m** with **7a** affords the corresponding cyclobutene product in 56% (Figure 2-6). This result gave only one possibility that alkene would be excited to its triplet state in photocatalysis.

To further determine the counterpart for the productive triplet excitation, radical clock experiments were performed (Scheme 2-7). Prepared each cyclopropyl alkyne **6l** and cyclopropyl maleimide **7y** was reacted with **7a** and **6a**, respectively. The reaction of **6l** with **7a** afforded the cyclobutene **8la** in 67% yield. However, the reaction of cyclopropyl maleimide 7y with 6a gave the isomerized product **7y'** along with cyclobutene **8ay** in low yields. Moreover, The reaction of cyclopropyl maleimide **7y** alone afforded **7y'** in 73% yield in the standard condition. On the contrary, no reaction was observed when

using cyclopropyl alkyne **6l** alone. The reason that the ring opening of **7y** occured during excitation while the cyclopropyl ring of triplet alkyne **6l** remains intact would be its less radical properties

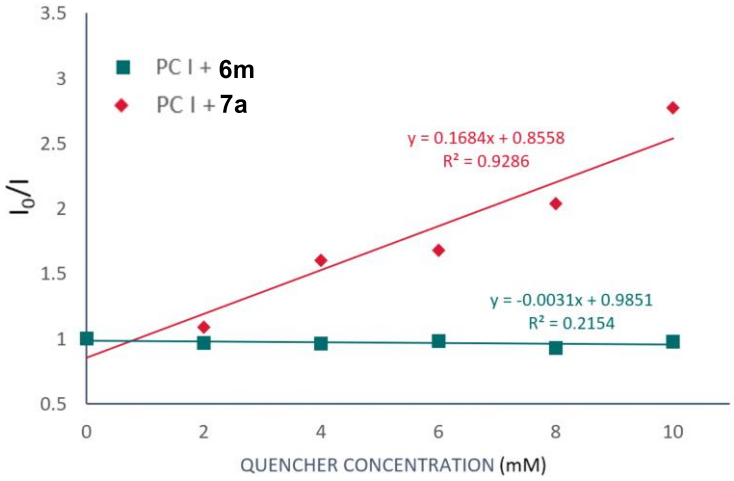
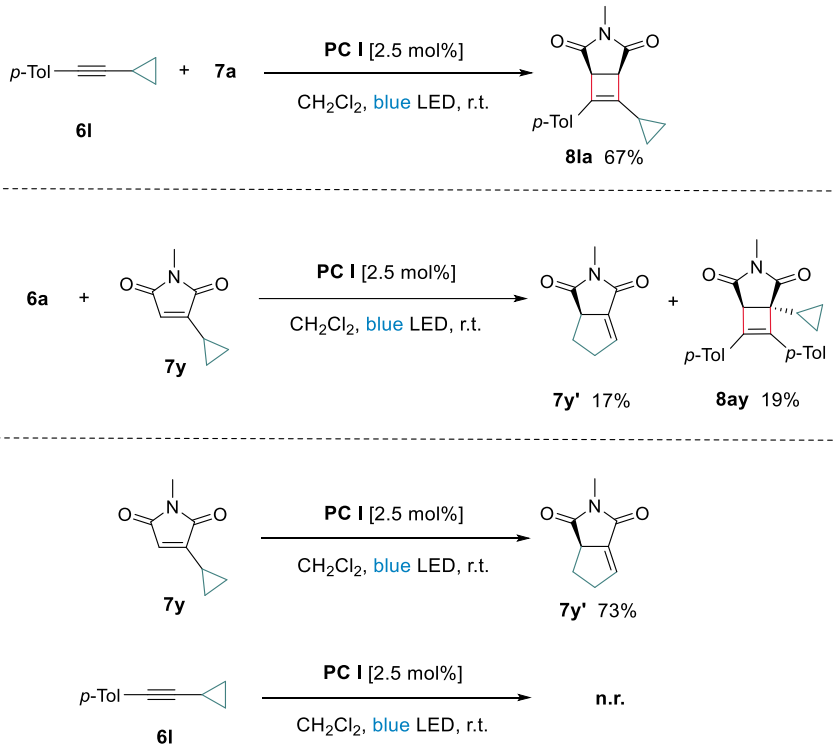


Figure 2-6. Stern-Vomer plot with 6m and 7a



Scheme 2-7. Radical clock experiments

on the carbon directly substituted cyclopropyl group of triplet alkyne **6l**. (The rate constant of ring

opening of α-(2-phenylcyclopropyl)vinyl radicals ((1.6 ± 0.2) × 10^{10} s^{-1}) was reported. It is higher than the one of its carbinyl radical (9.4 × 10^{7} s^{-1}))[43, 44]

We proposed a plausible reaction pathway based on above experiments (Figure 2-7). This is an energetically feasible process. Triplet energy transfer occurs from Ir photocatalyst to alkene **7a** under visible light. Triplet diradical intermediate **7a*** undergoes radical addition on to diarylalkynes **6a** to afford **Int-8aa**, which can be transformed to cyclobutene **8aa** after inter system crossing process.

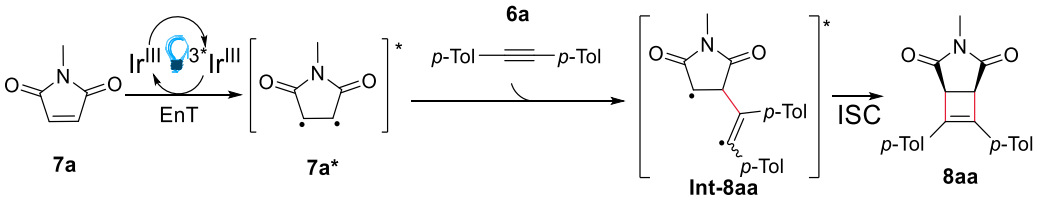


Figure 2-7. Reaction mechanism of intermolecular reaction

2.6. Conclusion

We achieved intermolecular [2+2] cycloaddition of alkyne with alkene through triplet energy transfer under visible light. The synthesis of cyclobutenes was attained in the intermolecular reactions. It is worth pointing out that alkene undergoes cycloaddition with alkyne overcoming dimerization although alkene dimerization in photocatalysis is well known. The intermolecular reaction of a wide range of alkynes with alkenes including electron deficient groups underwent smoothly to give the corresponding cycloadducts. Mono-activated acyclic alkenes fail to form cyclobutene products but we accomplished the mono-activated alkene reaction with cyclic forms such as coumarin. We can infer from a variety of experiments that between alkynes and alkenes, alkenes react with alkynes, which is ground state, through productive activation to its triplet state. Moreover, we attained successful synthetic applications of cyclobutene such as rearrangement, ozonolysis, epoxidation and 4π electrocyclic ring opening to give good accessibilities toward complex molecules.

2.7. Experimental Procedure and Data

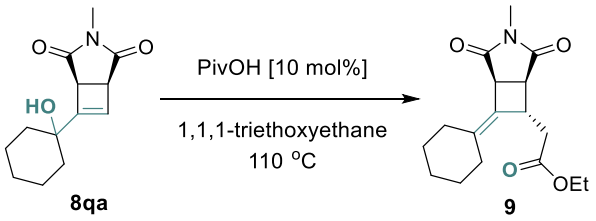
Optimization procedure : In a dried 4 mL vial, di(*p*-tolyl)acetylene **6a** (0.05 mmol, 1.0 equiv.), *N*-methylmaleimide **7a** (1.5 equiv.), and catalyst Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (**PC I**) were added. The heterogenic mixture was dissolved in solvents under Ar gas in glovebox. And then the solution was

irradiated under 12 W blue LED strip at ambient temperature maintained with a cooling fan. The solution was put under nitrogen blow after finishing reaction with monitoring by TLC technique. ^{1}H NMR analysis decided the yield of desired product from the mixture using trichloroethylene as the internal standard in $CDCl_3$.

General procedure A **(cyclobutenes synthesis)**

In a dried 4 mL vial, alkyne (1.0 equiv., 0.1 mmol), alkene (1.5 equiv.), and photocatalyst $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5 mol%) were added. The heterogenic mixture was dissolved in CH_2Cl_2 (2 mL) under Ar gas in glovebox. The solution was then irradiated under 12 W blue LED strip at ambient temperature maintained with a cooling fan. The solution was put under nitrogen blow after finishing reaction with monitoring by TLC technique. Column Flash chromatography separated the residue on silica gel to obtain desired product.

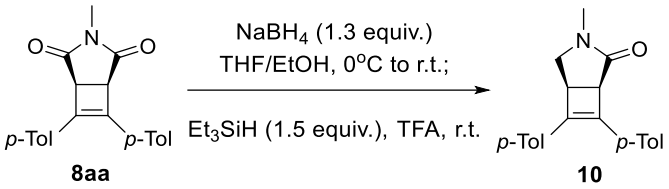
Synthetic applications



8qa **9**

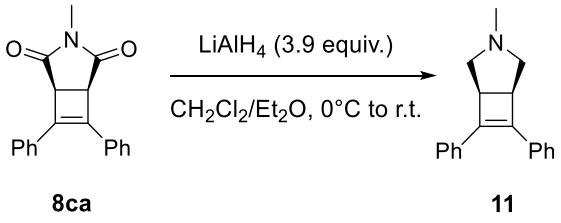
To a solution of cyclobutene **8qa** (0.1 mmol, 1.0 equiv.) in triethyl orthoacetate (0.2 M, 0.5 mL) was added a catalytic quantity of trimethylacetic acid (0.1 equiv.) at rt. The solution was stirred at 110 °C for 1 day. The solution was washed using saturated aqueous $NaHCO_3$ and extracted using CH_2Cl_2. The collected DCM solution was dehydrated using sodium sulfate anhydrous, filtered and dried under vacuum. Flash chromatography separated the residue using silica column to give the desired product **9**. 18 mg, 60% yield; colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.16 (q, J = 7.1 Hz, 2H), 3.90 (d, J = 6.1 Hz, 1H), 3.34 (d, J = 3.5 Hz, 1H), 3.14 (dd, J = 6.1, 3.0 Hz, 1H), 2.97 (s, 3H), 2.74 (dd, J = 15.5, 4.2 Hz, 1H), 2.60 (dd, J = 15.5, 9.3 Hz, 1H), 2.21 (s, 2H), 2.00 – 1.85 (m, 2H), 1.49 (s, 6H), 1.27 (t, J = 7.5 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0, 176.3, 170.9, 141.8, 121.9, 60.7, 45.4, 41.5, 41.0, 38.5, 30.0, 29.6, 27.5, 27.4, 26.0, 25.1, 14.2; HRMS *m/z* calculated for $[C_{17}H_{24}NO_4]^+$ ($[M+H]^+$): 306.1700, observed 306.1701.

Synthesis of 3-methyl-6,7-di-*p*-tolyl-3-azabicyclo[3.2.0]hept-6-en-2-one (10)



To a solution of cyclobutene **8aa** (1.0 equiv., 0.1 mmol) in dry THF/EtOH (0.1 M, 0.3 mL/0.7 mL) was slowly added $NaBH_4$ (1.3 equiv.) at 0 °C under N_2 flow and stirred the mixture overnight at room temperature. When TLC indicated the reaction was complete, the solution was adjusted to slightly acidic pH with glacial acetic acid (few drops), then concentrated *in vacuo*. The resulting mixture was diluted in EtOAc, washed with sat. $NaHCO_3$ solution and extracted with EtOAc. The collected EA solution was dehydrated using sodium sulfate anhydrous, filtered and evaporated the solvent in vacuo. To the hydroxylactam prepared above was added triethylsilane (1.5 equiv.) followed by TFA (0.5 mL, 0.2 M). The reaction was stirred at rt for overnight under nitrogen flow. When TLC indicated the process was complete, the solvent was evaporated in vacuo. Flash chromatography separated the residue using silica column to obtain desired product. 21 mg, 69% yield; white solid; m.p. 88 – 90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.1 Hz, 2H), 7.42 (d, *J* = 7.9 Hz, 2H), 7.17 (d, *J* = 7.9 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 3.72 (d, *J* = 4.2 Hz, 1H), 3.66 (ddd, *J* = 8.4, 4.4, 2.0 Hz, 1H), 3.49 (dd, *J* = 10.2, 8.4 Hz, 1H), 3.33 (dt, *J* = 10.2, 1.8 Hz, 1H), 2.80 (s, 3H), 2.37 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.2, 140.9, 139.6, 138.0, 137.8, 131.4, 130.4, 129.4, 129.0, 126.4, 126.3, 49.0, 46.6, 34.0, 29.7, 21.0, 21.0; HRMS *m/z* calculated for $[C_{21}H_{22}NO]^+$ ($[M+H]^+$): 304.1696, observed : 304.1697

Synthesis of 3-methyl-6,7-diphenyl-3-azabicyclo[3.2.0]hept-6-ene (11)



To a slurry of $LiAlH_4$ (3.9 equiv.) in Et_2O (0.25 mL, 0.2 M) was added solution of cyclobutene **8ca** (0.05 mmol, 1.0 equiv.) in CH_2Cl_2 (0.5 mL, 0.1 M) at 0°C under nitrogen. The mixture was stirred at room temperature for 1 hour, and H_2O was carefully added at 0 °C. To reaction suspension was hydrated using Na_2SO_4, filtered and evaporated the solvent in vacuo. Column Flash chromatography separated the residue on silica gel to give the desired product. 9 mg, 69% yield; yellow oil; ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.59 – 7.54 (m, 4H), 7.34 – 7.28 (m, 4H), 7.27 – 7.21 (m, 2H), 3.54 (d, *J* = 6.0 Hz, 2H), 3.14 (d, *J* = 9.9 Hz, 2H), 2.36 (s, 3H), 2.08 – 1.98 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 134.4, 128.4, 128.0, 126.5, 55.5, 44.1, 42.2.; HRMS *m/z* calculated for $[C_{19}H_{20}N]^+$ ($[M+H]^+$): 262.1590, observed 262.1592.

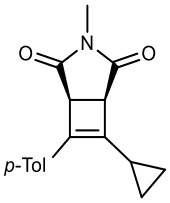
Effect of Triplet Quencher

In an dried 4 mL vial, di(*p*-tolyl)acetylene **6a** (0.05 mmol, 1.0 equiv.), *N*-methylmaleimide **7a** (1.5 equiv.), photocatalyst $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5 mol%) and triplet quencher benzil (1.0 equiv.) were equipped. The combined materials were dissolved in CH_2Cl_2 (2 mL) under argon atmosphere in glovebox. The reaction mixture was then irradiated by 12 W blue LED lamp at room temperature (maintained with a cooling fan) for 4 hours. Under reduced pressure, the solvent was evaporated. ^1H NMR analysis decided the yield of desired product from the mixture using trichloroethylene as the internal standard in $CDCl_3$; 30% yield.

Radical Clock Experiments

a)

6-cyclopropyl-3-methyl-7-(*p*-tolyl)-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (**8la**)



Prepared according to the ***General Procedure A*** using 1-(cyclopropylethynyl)-4-methylbenzene **6l** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 18 mg, 67% yield; white solid; m.p. 98 – 100 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 8.3 Hz, 2H), 3.89 (d, *J* = 3.5, 1H), 3.50 (d, *J* = 3.5 Hz, 1H), 2.94 (s, 3H), 2.35 (s, 3H), 1.96 – 1.89 (m, 1H), 1.16 – 1.10 (m, 1H), 1.00 – 0.80 (m, 3H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 175.5, 143.1, 138.8, 138.2, 130.5, 129.5, 126.3, 43.8, 24.9, 21.5, 11.4, 6.8, 6.5; HRMS *m/z* calculated for $[C_{17}H_{18}NO_2]^+$ ($[M+H]^+$): 268.1332, observed : 268.1334

b)

Di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.), 3-cyclopropyl-1-methyl-1H-pyrrole-2,5-dione **7y** (1.5 equiv.), and photocatalyst $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5 mol%) were added to an oven-dried 4 mL vial equipped with a stir bar. The combined materials were dissolved in CH_2Cl_2 (2 mL) under argon atmosphere in glovebox. The reaction mixture was then irradiated by 12 W blue LED lamp at room temperature (maintained with a cooling fan) for 48 hours. the solvent was evaporated in vacuo. Flash chromatography separated the residue using silica column to give **8ay** (19% yield) and **7y′** (17% yield).

c)

3-cyclopropyl-1-methyl-1H-pyrrole-2,5-dione **7y** (1.0 equiv.) and photocatalyst $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5 mol%) were added to an oven-dried 4mL vial equipped with a stir bar. The combined materials were dissolved in CH_2Cl_2 (2 mL) under argon atmosphere in glovebox. The reaction mixture was then irradiated by 12 W blue LED lamp at room temperature (maintained with a cooling fan) for 4 hours. the solvent was evaporated in vacuo. Flash chromatography separated the residue using silica column to give **7y′** (73% yield).

1-(cyclopropylethynyl)-4-methylbenzene **6l** (0.1 mmol, 1.0 equiv.) and photocatalyst $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5 mol%) were added to an oven-dried 4mL vial equipped with a stir bar. The combined materials were dissolved in CH_2Cl_2 (2 mL) under argon atmosphere in glovebox. The reaction mixture was then irradiated by 12 W blue LED lamp at room temperature (maintained with a cooling fan) for 48 hours. the solvent was evaporated in vacuo. The reaction wasn't processed. (By using ^1H NMR analysis of residues, the result was decided in $CDCl_3$.)

Quantum Yield Measurement

Determination of the light intensity at 436 nm

The effective photon flux of the used fluorometer was determined using standard ferrioxalate actinometry. A 0.15 M ferrioxalate solution was prepared by dissolving potassium ferrioxalate hydrate (221 mg, 0.45 mmol) in 0.05 M H_2SO_4 (3 mL). A buffer solution of 1,10-phenanthroline was prepared by dissolving 1,10-phenanthroline (10 mg, 0.055 mmol) and sodium acetate (2.25 g) in 0.5 M H_2SO_4 (10 mL). The ferrioxalate solution (0.4 mL) was added to cuvette and was irradiated at 436 nm for 90 s in the fluorometer. After irradiation, the phenanthroline solution (0.07 mL) was added to the cuvette and the mixture was allowed in the absence of light for 1 h to achieve full phenanthroline coordination to the ferrous ions. In addition, a non-irradiated sample was prepared similarly.

The absorbance of both samples was measured at 510 nm. From these values, conversion could be determined using Lambert-Beer's law :

$$\boldsymbol{n}\left(\mathbf{Fe^{2+}}\right) = \frac{\mathrm{V} \cdot \boldsymbol{\Delta A}}{\boldsymbol{l} \cdot \boldsymbol{\varepsilon}} \quad (1)$$

Where V is the total volume (0.47 mL) of the solution after addition of phenanthroline, l is the optical path length of the cuvette (1.00 cm), ε is the molar absorptivity of the ferrioxalate actinometer (11,100 L mol^{-1} cm^{-1}) and ΔA is the absorbance difference between the irradiated at 436 nm and non-irradiated sample (1.305).

From this value, the photon flux Φ_q in the system can be calculated as :

$$\boldsymbol{\Phi_q} = \frac{\boldsymbol{n}\left(\mathbf{Fe^{2+}}\right)}{\boldsymbol{\Phi_F} \cdot \boldsymbol{t} \cdot \boldsymbol{f}} \quad (2)$$

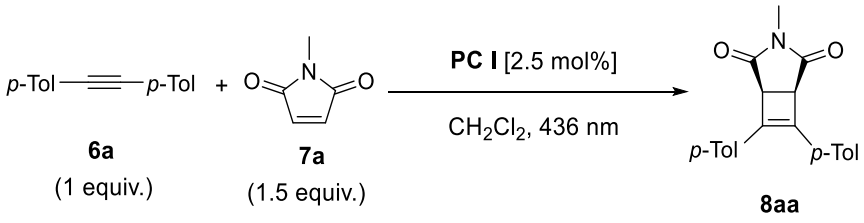
Where Φ_F is the quantum yield of the ferrioxalate system (1.01 for 0.15 M solution at λ_{ex} = 436 nm), t is the irradiation time (90.0 s) and f is the fraction of light absorbed at λ_{ex} = 436 nm (0.9987, See Supplementary Equation 3). The absorption fraction is calculated as :

$$f = 1\text{-}10^{-A} \quad (3)$$

Where A in Supplementary Equation 3 is the measured absorbance of ferrioxalate solution at 436 nm. It was measured to be 2.873.

The photon flux Φ_q was calculated (average of two experiments) to be 6.09×10^{-10} einstein s^{-1}.

Determination of quantum yield



A cuvette was charged with alkyne **6a** (0.025 mmol, 1 equiv.), alkene **7a** (2 equiv.), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5 mol%), and CH_2Cl_2 (0.5 mL, 0.05 M) in Ar charged glovebox. The sample was sealed with parafilm and irradiated (λ = 436 nm, slit width = 20.0 nm) for 7,200 s (2 h). After irradiation, the solvent was evaporated with a stream of nitrogen. The yield of product **8aa** formed was determined by ^{1}H NMR based on a trichloroethylene as internal standard. The quantum yield (average of two experiments) was determined using Supplementary Equation 4.

$$\boldsymbol{\Phi} = \frac{\boldsymbol{n(product)}}{\boldsymbol{\Phi_q \cdot t \cdot f}} \quad (4)$$

The absorbance of photocatalyst in CH_2Cl_2 was measured at the reaction concentration of 1.25×10^{-3} M. The absorbance at 436 nm is 1.91 indicating the fraction of light absorbed (*f*) is 0.9877.

The quantum yield Φ was calculated (The yields of product 3aa are 15% and 16% in two experiments) to be 0.91.

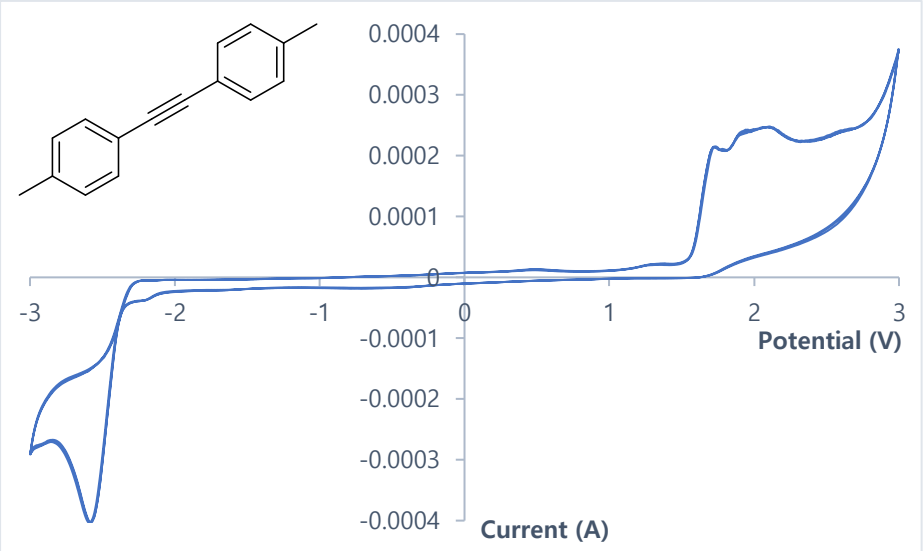
Stern-Volmer luminescence quenching experiments

Stern-Volmer luminescence quenching studies were carried out using a 0.1 mM solution of photocatalyst and variable concentrations of substrate in dry DCM under Ar gas at rt. The samples were prepared in 0.5 mL quartz cuvettes inside an argon filled glove-box, and sealed with parafilm. The solutions were irradiated at 420 nm and the luminescence was measured at maximum emission wavelength of each photocatalyst. (I_0 = emission intensity of the photocatalyst in isolation at the specified wavelength; I = observed intensity as a function of the quencher concentration)

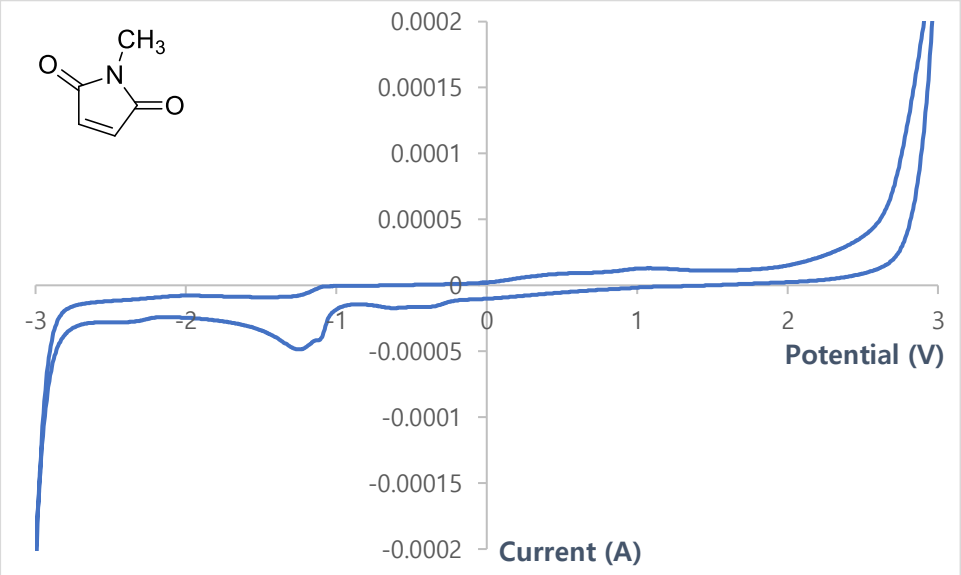
Electrochemical measurements with cyclic voltammogram

Electrochemical measurement :

Samples for electrochemical measurements were prepared with 0.03 mmol of substrate in anhydrous degassed 0.1 M Bu_4NPF_6 solution in MeCN (3 mL). The corresponding cyclic voltammograms were collected by a Potentiostat equipped with reference electrode (3 M KCl Ag/AgCl), counter electrode (platinum wire) and working electrode (glassy carbon), and 100 mV/s (scan rate); Data were analyzed by subtracting the electrolyte solution background current prior to identifying the maximum current (Cp) and determining the potential ($E_{p/2}$) at half this value ($C_{p/2}$). The obtained value was referenced to Ag/AgCl and converted to SCE by subtracting 0.04 V.

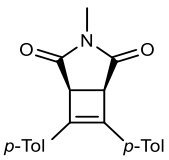


$E_{p/2}^{ox}$ = +1.59 V vs SCE, $E_{p/2}^{red}$ = -2.50 V vs SCE



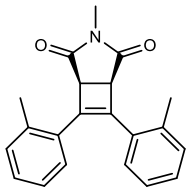
$E_{p/2}^{red}$ = -1.16 V vs SCE

3-methyl-6,7-di-*p*-tolyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8aa)



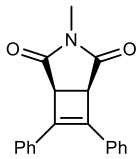
Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 24 mg, 76% yield; white solid; m.p. 134 – 135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.2 Hz, 4H), 7.18 (d, *J* = 7.9 Hz, 4H), 4.06 (s, 2H), 2.97 (s, 3H), 2.37 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 139.2, 138.3, 130.3, 129.3, 126.8, 44.9, 24.8, 21.4; HRMS *m/z* calculated for $[C_{21}H_{20}NO_2]^+$ ($[M+H]^+$): 318.1489, observed : 318.1490

3-methyl-6,7-di-*o*-tolyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8ba)



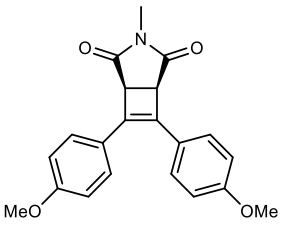
Prepared according to the ***General Procedure A*** using 1,2-di-*o*-tolylethyne **6b** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 30 mg, 95% yield; white solid; m.p. 202 – 203 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 7.2, 1.7 Hz, 2H), 7.25 – 7.12 (m, 6H), 4.16 (s, 2H), 3.02 (s, 3H), 2.01 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 141.9, 136.4, 133.7, 130.8, 129.0, 128.5, 126.0, 47.1, 25.1, 20.9; HRMS *m/z* calculated for $[C_{21}H_{20}NO_2]^+$ ($[M+H]^+$): 318.1489, observed : 318.1491

3-methyl-6,7-diphenyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8ca)



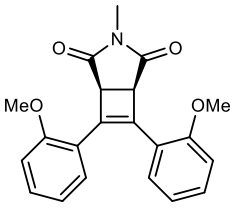
Prepared according to the ***General Procedure A*** using 1,2-diphenylethyne **6c** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 18 mg, 62% yield; white solid; m.p. 129 – 130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.73 (m, 4H), 7.41 – 7.31 (m, 6H), 4.10 (s, 2H), 2.98 (s, 3H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 139.4, 133.0, 129.4, 128.8, 127.0, 45.2, 25.0; HRMS *m/z* calculated for $[C_{19}H_{16}NO_2]^+$ ($[M+H]^+$): 290.1176, observed : 290.1183

6,7-bis(4-methoxyphenyl)-3-methyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8da)



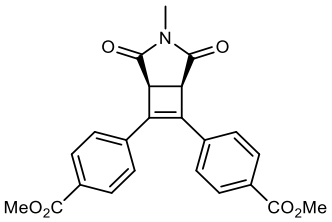
Prepared according to the ***General Procedure A*** using 1,2-bis(4-methoxyphenyl)ethyne **6d** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 19 mg, 54% yield; white solid; m.p. 131 – 132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.9 Hz, 4H), 6.90 (d, *J* = 8.9 Hz, 4H), 4.04 (s, 2H), 3.83 (s, 6H), 2.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 160.1, 136.7, 128.4, 126.1, 114.2, 55.5, 45.0, 24.9; HRMS *m/z* calculated for $[C_{21}H_{20}NO_4]^+$ ($[M+H]^+$): 350.1387, observed : 350.1389

6,7-bis(2-methoxyphenyl)-3-methyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8ea)



Prepared according to the ***General Procedure A*** using 1,2-bis(2-methoxyphenyl)ethyne **6e** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 17 mg, 49% yield; white solid; m.p. 178 – 179 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 7.6, 1.7 Hz, 2H), 7.27 (ddd, *J* = 8.3, 7.4, 1.7 Hz, 2H), 6.93 (td, *J* = 7.5, 1.0 Hz, 2H), 6.83 (d, *J* = 8.3 Hz, 2H), 4.19 (s, 2H), 3.53 (s, 6H), 2.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 157.3, 138.0, 129.9, 129.5, 123.7, 120.0, 110.3, 54.9, 46.9, 24.9; HRMS *m/z* calculated for $[C_{21}H_{20}NO_4]^+$ ($[M+H]^+$): 350.1387 , observed : 350.1387

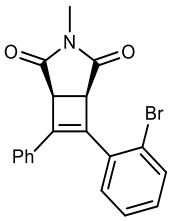
Dimethyl 4,4'-(3-methyl-2,4-dioxo-3-azabicyclo[3.2.0]hept-6-ene-6,7-diyl)dibenzoate (8fa)



Prepared according to the ***General Procedure A*** using dimethyl 4,4'-(ethyne-1,2-diyl)dibenzoate **6f** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 30 mg, 74% yield; white solid; m.p. 207 –

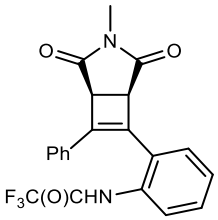
209 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.7 Hz, 4H), 7.80 (d, *J* = 8.7 Hz, 4H), 4.17 (s, 2H), 3.94 (s, 6H), 3.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 166.5, 140.7, 136.6, 130.9, 130.2, 127.1, 52.4, 45.4, 25.2; HRMS *m/z* calculated for $[C_{23}H_{20}NO_6]^+$ ($[M+H]^+$): 406.1285, observed : 406.1297

6-(2-bromophenyl)-3-methyl-7-phenyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8ga)



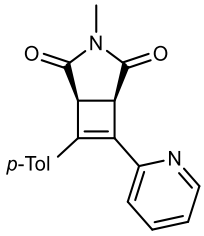
Prepared according to the ***General Procedure A*** using 1-bromo-2-(phenylethynyl)benzene **6g** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 26 mg, 71% yield; white solid; m.p. 150 – 151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.0 Hz, 1H), 7.48 – 7.46 (m, 2H), 7.38 – 7.23 (m, 6H), 4.30 (d, *J* = 3.4 Hz, 1H), 4.18 (d, *J* = 3.4 Hz, 1H), 3.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.8, 174.6, 143.2, 138.7, 134.6, 133.4, 132.1, 130.5, 130.2, 129.5, 128.7, 127.8, 127.0, 122.6, 47.4, 45.2, 25.0; HRMS *m/z* calculated for $[C_{19}H_{15}BrNO_2]^+$ ($[M+H]^+$): 368.0281, observed : 368.0281

3-methyl-6-phenyl-7-(2-((trifluoromethoxy)amino)phenyl)-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8ha)



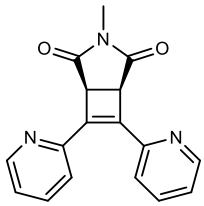
Prepared according to the ***General Procedure A*** using 2,2,2-trifluoro-*N*-(2-(phenylethynyl)phenyl)acetamide **6h** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 35 mg, 88% yield; yellow viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) 8.38 (s, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.51 – 7.41 (m, 3H), 7.40 – 7.35 (m, 3H), 7.32 (t, *J* = 7.6 Hz, 1H), 4.21 (d, *J* = 3.5 Hz, 1H), 4.15 (d, *J* = 3.5 Hz, 1H), 3.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ175.3, 174.0, 143.0, 134.6, 131.7, 131.5, 130.31, 130.26, 129.0, 128.7, 127.0, 125.91, 125.90, 124.2, 46.2, 45.6, 25.1; HRMS *m/z* calculated for $[C_{21}H_{15}F_3N_2NaO_3]^+$ ($[M+Na]^+$): 423.0927, observed : 423.0932.

3-methyl-6-(pyridin-2-yl)-7-(*p*-tolyl)-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8ia)



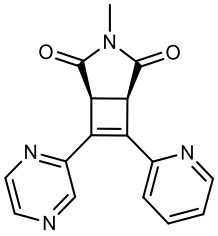
Prepared according to the ***General Procedure A*** using 2-(*p*-tolylethynyl)pyridine **6i** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 16 mg, 53% yield; white solid; m.p. 171 – 173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (ddd, *J* = 4.8, 1.8, 1.0 Hz, 1H), 8.42 (d, *J* = 8.3 Hz, 2H), 7.83 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.80 – 7.75 (m, 1H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.23 (ddd, *J* = 7.4, 4.8, 1.3 Hz, 1H), 4.19 (d, *J* = 3.7 Hz, 1H), 4.15 (d, *J* = 3.7 Hz, 1H), 2.97 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 174.8, 151.7, 149.4, 143.7, 140.3, 136.6, 136.2, 129.7, 129.1, 122.9, 122.7, 44.6, 43.9, 24.8, 21.6; HRMS *m/z* calculated for $[C_{19}H_{17}N_2O_2]^+$ ($[M+H]^+$): 305.1285, observed : 305.1298

3-methyl-6,7-di(pyridin-2-yl)-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8ja)



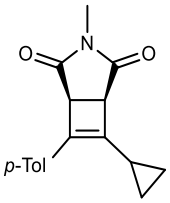
Prepared according to the ***General Procedure A*** using 1,2-di(pyridin-2-yl)ethyne **6j** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 15 mg, 51% yield; pale yellow solid; m.p. 212 – 214 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 – 8.76 (m, 2H), 8.61 (d, *J* = 7.9 Hz, 2H), 7.80 (td, *J* = 7.8, 1.9 Hz, 2H), 7.29 – 7.26 (m, 2H), 4.33 (s, 2H), 2.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 151.0, 149.7, 142.2, 136.6, 124.8, 123.7, 44.4, 25.1; HRMS *m/z* calculated for $[C_{17}H_{13}N_3NaO_2]^+$ ($[M+Na]^+$): 314.0900 , observed : 314.0899

3-methyl-6-(pyrazin-2-yl)-7-(pyridin-2-yl)-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8ka)



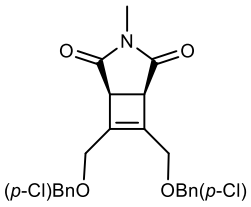
Prepared according to the ***General Procedure A*** using 2-(pyridin-2-ylethynyl)pyrazine **6k** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 15 mg, 51% yield; pale yellow solid; m.p. 222 – 223 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.23 (s, 1H), 8.79– 8.78 (m, 1H), 8.73 (m, 1H), 8.55– 8.53 (m, 1H), 8.19 (d, *J* = 7.9 Hz, 1H), 7.84 (td, *J* = 7.8, 1.8 Hz, 1H), 7.32 (ddd, 7.6, 4.8. 1.1 Hz, 1H), 4.41 (d, *J* = 3.6 Hz, 1H), 4.30 (d, *J* = 3.6 Hz, 1H), 2.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 173.9, 150.6, 150.0, 147.0, 144.1, 143.9, 137.0, 132.2, 128.7, 124.4, 124.3, 121.6, 44.8, 44.1, 25.2; HRMS *m/z* calculated for $[C_{16}H_{13}N_4O_2]^+$ ($[M+H]^+$): 293.1033, observed : 293.1033

6-cyclopropyl-3-methyl-7-(*p*-tolyl)-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (**8la**)



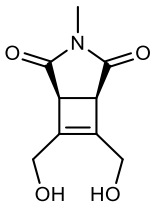
Prepared according to the ***General Procedure A*** using 1-(cyclopropylethynyl)-4-methylbenzene **6l** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 18 mg, 67% yield; white solid; m.p. 98 – 100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 8.3 Hz, 2H), 3.89 (d, *J* = 3.5, 1H), 3.50 (d, *J* = 3.5 Hz, 1H), 2.94 (s, 3H), 2.35 (s, 3H), 1.96 – 1.89 (m, 1H), 1.16 – 1.10 (m, 1H), 1.00 – 0.80 (m, 3H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 175.5, 143.1, 138.8, 138.2, 130.5, 129.5, 126.3, 43.8, 24.9, 21.5, 11.4, 6.8, 6.5; HRMS *m/z* calculated for $[C_{17}H_{18}NO_2]^+$ ($[M+H]^+$): 268.1332, observed : 268.1334

6,7-bis(((4-chlorobenzyl)oxy)methyl)-3-methyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (**8ma**)



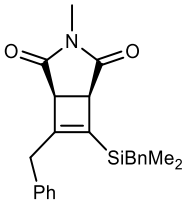
Prepared according to the ***General Procedure A*** using 1,4-bis((4-chlorobenzyl)oxy)but-2-yne **6m** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 25 mg, 56% yield; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.4 Hz, 4H), 7.24 (d, *J* = 8.3 Hz, 4H), 4.48 (s, 4H), 4.17 (d, *J* = 13.1 Hz, 2H), 4.09 (d, *J* = 13.2 Hz, 2H), 3.73 (s, 2H), 2.95 (s, 3H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 142.7, 136.2, 133.7, 129.1, 128.8, 72.5, 65.3, 45.4, 24.9; HRMS *m/z* calculated for $[C_{23}H_{21}Cl_2NNaO_4]^+$ ($[M+Na]^+$): 468.0740, observed : 468.0740

6,7-bis(hydroxymethyl)-3-methyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8na)



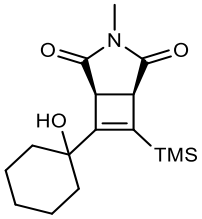
Prepared according to the ***General Procedure A*** using but-2-yne-1,4-diol (0.1 mmol, 1.0 equiv.) **6n** and *N*-methylmaleimide **7a** (1.5 equiv.), 18 mg, 91% yield; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.34 (s, 4H), 3.68 (s, 2H), 2.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 142.5, 58.7, 44.7, 24.8; HRMS *m/z* calculated for $[C_9H_{11}NNaO_4]^+$ ($[M+Na]^+$): 220.0580, observed : 220.0580

6-benzyl-7-(benzyldimethylsilyl)-3-methyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8oa)



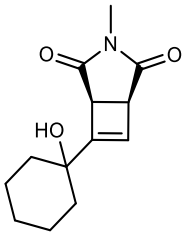
Prepared according to the ***General Procedure A*** using benzyldimethyl(3-phenylprop-1-yn-1-yl)silane **6o** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 27 mg, 72% yield; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.28 (m, 2H), 7.24 – 7.18 (m, 3H), 7.12 – 7.07 (m, 3H), 6.95 – 6.92 (m, 2H), 3.61 (d, *J* = 3.2 Hz, 1H), 3.44 (d, *J* = 3.2 Hz, 1H), 3.26 (s, 2H), 2.96 (s, 3H), 2.22 (d, *J* = 2.6 Hz, 2H), 0.23 (s, 3H), 0.19 (s, 3H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 174.7, 162.7, 146.6, 139.1, 136.7, 129.0, 128.9, 128.4, 128.3, 126.8, 124.5, 48.8, 45.1, 37.5, 25.5, 24.8, -2.9, -3.0; HRMS *m/z* calculated for $[C_{23}H_{25}NNaO_2Si]^+$ ($[M+Na]^+$): 398.1547, observed : 398.1548

6-(1-hydroxycyclohexyl)-3-methyl-7-(trimethylsilyl)-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8pa)



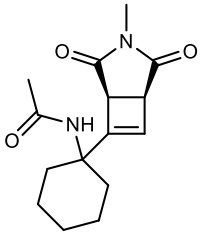
Prepared according to the ***General Procedure A*** using 1-((trimethylsilyl)ethynyl)cyclohexan-1-ol **6p** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 29 mg, 94% yield; white solid; m.p. 89 – 91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.83 (d, *J* = 3.2 Hz, 1H), 3.48 (d, *J* = 3.2 Hz, 1H), 2.95 (s, 3H), 1.72 – 1.49 (m, 9H), 1.30 – 1.16 (m, 1H), 0.21 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 175.8, 168.0, 146.2, 72.7, 47.1, 43.8, 36.4, 36.0, 25.2, 25.0, 21.24, 21.18, -0.4; HRMS *m/z* calculated for $[C_{16}H_{26}NO_3Si]^+$ ($[M+H]^+$): 308.1676, observed 308.1679.

6-(1-hydroxycyclohexyl)-3-methyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8qa)



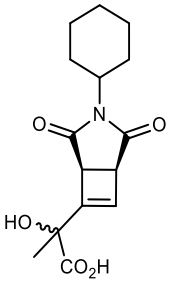
Prepared according to the ***General Procedure A*** using 1-ethynylcyclohexan-1-ol **6q** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 14 mg, 60% yield; white solid; m.p. 120 – 122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.18 (d, *J* = 1.1 Hz, 1H), 3.85 (d, *J* = 3.2 Hz, 1H), 3.63 (dd, *J* = 3.2, 1.0 Hz, 1H), 2.97 (s, 3H), 1.69 – 1.28 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 175.2, 158.3, 128.3, 71.0, 46.4, 43.1, 35.9, 35.2, 25.4, 25.1, 21.8, 21.7; HRMS *m/z* calculated for $[C_{13}H_{18}NO_3]^+$ ($[M+H]^+$): 236.1281, observed : 236.1289

***N*-(1-(3-methyl-2,4-dioxo-3-azabicyclo[3.2.0]hept-6-en-6-yl)cyclohexyl)acetamide (8ra)**



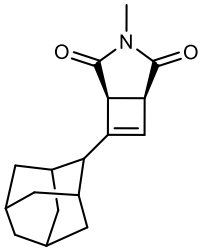
Prepared according to the ***General Procedure A*** using *N*-(1-ethynylcyclohexyl)acetamide **6r** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 27 mg, 98% yield; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.16 (d, *J* = 1.2 Hz, 1H), 5.48 (br s, 1 H), 3.71 (d, *J* = 3.2 Hz, 1H), 3.61 (dd, *J* = 3.2, 1.2 Hz, 1H), 2.93 (s, 3H), 2.09 – 2.02 (m, 2H), 1.97 (s, 3H), 1.62 – 1.26 (m, 8H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 175.3, 169.8, 156.0, 128.7, 55.3, 46.7, 42.9, 33.4, 33.1, 25.3, 25.0, 24.1, 21.5, 21.4; HRMS *m/z* calculated for $[C_{15}H_{20}N_2NaO_3]^+$ ($[M+Na]^+$): 299.1366, observed : 299.1366

2-(3-cyclohexyl-2,4-dioxo-3-azabicyclo[3.2.0]hept-6-en-6-yl)-2-hydroxypropanoic acid (8si)



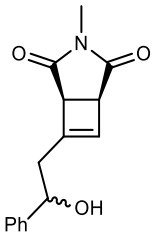
Prepared according to the ***General Procedure A*** using 2-hydroxy-2-methylbut-3-ynoic acid **6s** (0.1 mmol, 1.0 equiv.) and 1-cyclohexyl-1*H*-pyrrole-2,5-dione **7i** (1.5 equiv.), 25 mg, 85% yield (d.r. = 1.3:1); pale yellow solid; The NMR spectrum was obtained on a partially purified material as a mixture of diastereomers; ^{1}H NMR (400 MHz, CD_3OD) δ 6.31 (dd, *J* = 4.8, 1.1 Hz, 2H), 3.92 – 3.82 (m, 3H), 3.74 (d, *J* = 3.2 Hz, 1H), 3.5 (ddd, *J* = 5.5, 3.2, 1.0 Hz, 2H), 2.16 – 2.01 (m, 4H), 1.84 – 1.81 (m, 4H), 1.68 – 1.51 (m, 12H), 1.40 – 1.13 (m, 6H) ^{13}C NMR (100 MHz, CD_3OD) δ 177.8, 177.7, 177.5, 177.4, 177.11, 177.07, 156.2, 155.7, 131.7, 131.5, 75.5, 72.6, 52.7, 52.7, 48.0, 47.6, 44.0, 44.0, 29.6, 29.5, 29.5, 27.02, 27.00, 26.3, 24.6, 23.9; HRMS *m/z* calculated for $[C_{15}H_{19}NNaO_5]^+$ ($[M+Na]^+$): 316.1155, observed : 316.1155

6-((1*r*,3*r*,5*r*,7*r*)-adamantan-2-yl)-3-methyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8ta)



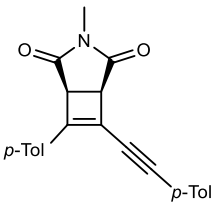
Prepared according to the ***General Procedure A*** using (3*r*,5*r*,7*r*)-1-ethynyladamantane **6t** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 13 mg, 48% yield; white solid; m.p. 138-139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.97 (d, *J* = 0.9 Hz, 1H), 3.76 (d, *J* = 3.2 Hz, 1H), 3.55 (dd, *J* = 3.2, 1.1 Hz, 1H), 2.95 (s, 3H), 2.00 (s, 3H), 1.77 – 1.62 (m, 12H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 175.4, 162.1, 125.8, 46.2, 43.1, 39.6, 36.5, 36.1, 27.8, 24.8; HRMS *m/z* calculated for $[C_{17}H_{22}NO_2]^+$ ($[M+H]^+$): 272.1645, observed 272.1645.

6-(2-hydroxy-2-phenylethyl)-3-methyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8ua)



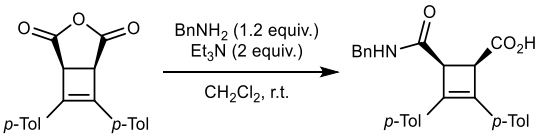
Prepared according to the ***General Procedure A*** using 1-phenylbut-3-yn-1-ol **6u** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 20 mg, 78% yield (d.r. = 1:1); pale yellow solid; m.p. 104 – 106 °C; The NMR spectrum was obtained on a partially purified material as a mixture of diastereomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.34 (m, 6.13H), 7.31 – 7.28 (m, 1.28H), 6.17 (d, *J* = 1.4 Hz, 1H), 6.14 (d, *J* = 1.4 Hz, 0.5H), 4.98 (dt, *J* = 7.9, 3.7 Hz, 1H), 4.89 (dt, *J* = 8.1, 3.9 Hz, 0.5H), 3.78 (d, *J* = 3.0 Hz, 0.5H), 3.74 (d, *J* = 2.8 Hz, 1H), 3.64 (m, 1.5H), 3.01 (d, *J* = 3.7 Hz, 0.5H), 2.96 (s, 1.5H), 2.91 (s, 3H), 2.73 – 2.57 (m, 3.4H), 2.39 (d, *J* = 4.1 Hz, 1H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 175.8, 175.5, 175.4, 150.5, 150.5, 143.5, 143.5, 132.4, 132.2, 128.7, 128.7, 128.0, 128.0, 125.8, 125.8, 71.8, 71.7, 49.2, 48.9, 44.7, 44.6, 39.9, 39.5, 25.0, 24.9; HRMS *m/z* calculated for $[C_{15}H_{15}NNaO_3]^+$ ($[M+Na]^+$): 280.0944, observed : 280.0944

3-methyl-6-(*p*-tolyl)-7-(*p*-tolylethynyl)-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8va)



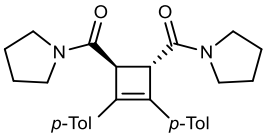
Prepared according to the ***General Procedure A*** using 1,4-di-*p*-tolylbuta-1,3-diyne **6v** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 24 mg, 70% yield; white solid; m.p. 163 – 165 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* =8.2 Hz, 2H), 7.43 (d, *J* = 8.1 Hz, 2H), 7.23 (d, *J* = 7.9 Hz, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 4.08 (d, *J* = 3.6 Hz, 1H), 3.95 (d, *J* = 3.6 Hz, 1H), 2.98 (s, 3H), 2.38 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 174.0, 148.6, 140.2, 139.5, 131.7, 129.6, 129.4, 129.2, 126.4, 119.2, 118.0, 99.3, 82.5, 46.6, 45.4, 24.9, 21.6, 21.6; HRMS *m/z* calculated for $[C_{23}H_{20}NO_2]^+$ ($[M+H]^+$): 342.1489, observed : 342.1490

4-(benzylcarbamoyl)-2,3-di-*p*-tolylcyclobut-2-ene-1-carboxylic acid (8ab′)



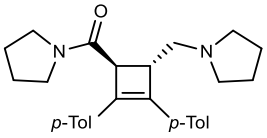
6,7-di-*p*-tolyl-3-oxabicyclo[3.2.0]hept-6-ene-2,4-dione **8ab** was prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and maleic anhydride (1.5 equiv.), and used without further purification. To a solution of 6,7-di-*p*-tolyl-3-oxabicyclo[3.2.0]hept-6-ene-2,4-dione **8ab** (1.0 equiv.) in CH_2Cl_2 (1 mL) was added Et_3N (0.2 mmol, 2.0 equiv.) and benzylamine (1.2 equiv.). The solution was stirred for 1 h, and then the mixture was concentrated *in vacuo*. Column Flash chromatography separated the residue on silica gel to afford the desired product., 40 mg, 97% yield; white solid; m.p. 189 – 190 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.09 (br s, 1H), 8.61 (t, *J* = 5.9 Hz, 1H), 7.45 (d, *J* = 8.1 Hz, 2H), 7.32 – 7.24 (m, 7H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 4.31 (dd, *J* = 5.9, 2.6 Hz, 2H), 4.12 – 4.09 (m, 2H), 2.31 (s, 3H), 2.30 (s, 3H) ^{13}C NMR (100 MHz, DMSO-d_6) δ 171.6, 169.7, 139.4, 137.8, 137.7, 137.5, 137.3, 131.5, 131.3, 129.0, 128.8, 128.2, 127.3, 126.73, 126.71, 126.1, 48.1, 45.1, 42.3, 29.9, 20.9; HRMS *m/z* calculated for $[C_{27}H_{25}NNaO_3]^+$ ($[M+Na]^+$): 434.1727, observed : 434.1734

(3,4-di-*p*-tolylcyclobut-3-ene-1,2-diyl)bis(pyrrolidin-1-ylmethanone) (8ac)



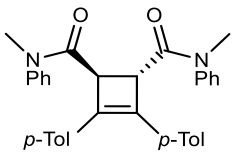
Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and *(E)*-1,4-di(pyrrolidin-1-yl)but-2-ene-1,4-dione **2c** (1.5 equiv.), 27 mg, 63% yield; white solid; m.p. 183 – 184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.1 Hz, 4H), 7.07 (d, *J* = 7.9 Hz, 4H), 4.21 (s, 2H), 3.58 – 3.51 (m, 6H), 3.48 – 3.42 (m, 2H), 2.31 (s, 6H), 1.95 – 1.82 (m, 8H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 139.3, 137.7, 131.8, 129.0, 126.5, 46.8, 46.5, 46.0, 26.2, 24.3, 21.4; HRMS *m/z* calculated for $[C_{28}H_{33}N_2O_2]^+$ ($[M+H]^+$): 429.2537, observed : 429.2542; The stereochemistry was confirmed by desymmetrization to **8ac′**

pyrrolidin-1-yl(4-(pyrrolidin-1-ylmethyl)-2,3-di-*p*-tolylcyclobut-2-en-1-yl)methanone (8ac′)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.1 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 7.8 Hz, 2H), 7.08 (d, *J* = 7.9 Hz, 2H), 4.14 (d, *J* = 1.5 Hz, 1H), 3.98 (dt, *J* = 10.0, 6.6 Hz, 1H), 3.79 (dt, *J* = 9.9, 2.0 Hz, 1H), 3.61 (dt, *J* = 10.0, 6.9 Hz, 1H), 3.53 (dt, *J* = 12.1, 7.1 Hz, 1H), 3.42 (ddd, *J* = 12.1, 7.5, 6.0 Hz, 1H), 3.36 – 3.30 (m, 1H), 3.27 – 3.21 (m, 1H), 3.01 – 2.91 (m, 2H), 2.81 – 2.75 (m, 1H), 2.73 – 2.66 (m, 1H), 2.36 (s, 3H), 2.32 (s, 3H), 2.21 – 2.16 (m, 2H), 1.95 – 1.74 (m, 6H); MS (APCI): *m/z* 416.0 $[M+H]^+$

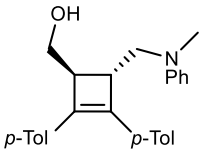
***N*^{1},*N*^{2}-dimethyl-*N*^{1},*N*^{2}-diphenyl-3,4-di-*p*-tolylcyclobut-3-ene-1,2-dicarboxamide (8ad)**



Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and *N*^{1},*N*^{4}-dimethyl-*N*^{1},*N*^{4}-diphenylmaleamide **7d** (1.5 equiv.), 27 mg, 54% yield; white solid; m.p. 167 – 169 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.29 (m, 6H), 7.19 – 6.99 (m, 12H), 3.96 (s, 2H), 3.20 (s, 6H), 2.32 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 143.4, 139.3, 137.7, 131.3, 129.7, 128.9,

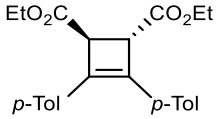
128.0, 127.2, 126.6, 46.0, 37.9, 21.4; HRMS *m/z* calculated for $[C_{34}H_{32}N_2NaO_2]^+$ ($[M+Na]^+$) : 523.2356, observed 523.2356; The stereochemistry was confirmed by desymmetrization to **8ad′**.

(4-((methyl(phenyl)amino)methyl)-2,3-di-*p*-tolylcyclobut-2-en-1-yl)methanol (8ad′)



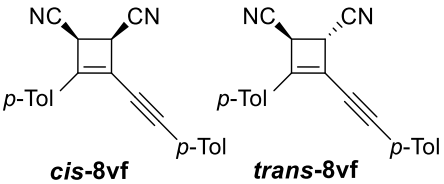
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.1 Hz, 4H), 7.28 – 7.24 (m, 2H), 7.15 – 7.11 (m, 4H), 6.79 (d, *J* = 7.9 Hz, 2H), 6.73 (t, *J* = 7.3 Hz, 1H), 3.85 (dd, *J* = 11.1, 4.4 Hz, 1H), 3.71 – 3.64 (m, 2H), 3.41 (dd, *J* = 14.7, 8.9 Hz, 1H), 3.31 (ddd, *J* = 8.8, 4.7, 1.5 Hz, 1H), 3.13 (ddd, *J* = 7.3, 4.3, 1.5 Hz, 1H), 2.90 (s, 3H), 2.36 (s, 3H), 2.34 (s, 3H); MS (APCI): *m/z* 384.1 $[M+H]^+$

Diethyl 3,4-di-*p*-tolylcyclobut-3-ene-1,2-dicarboxylate (8ae)



Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and Diethyl fumarate **7e** (1.5 equiv.), 19 mg, 51% yield; white solid; m.p. 91 – 93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.2 Hz, 4H), 7.12 (d, *J* = 7.9 Hz, 4H), 4.18 – 4.08 (m, 6H), 2.35 (s, 6H), 1.19 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 138.3, 138.0, 130.6, 129.0, 126.6, 60.9, 45.9, 21.4, 14.1; HRMS *m/z* calculated for $[C_{24}H_{27}O_4]^+$ ($[M+H]^+$): 379.1904, observed : 379.1918

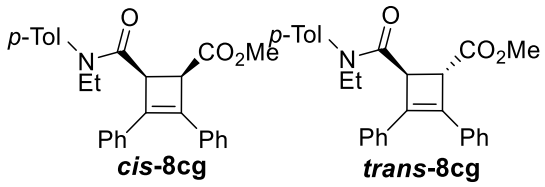
3-(*p*-tolyl)-4-(*p*-tolylethynyl)cyclobut-3-ene-1,2-dicarbonitrile (8vf)



Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and fumaronitrile (1.5 equiv.), 16 mg, 51% yield, (*cis*/*trans* 1.3:1); **(*cis*-8vf)**: yellow solid; m.p. 163 –

164 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.1 Hz, 2H), 7.45 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 7.21 (d, *J* = 7.9 Hz, 2H), 4.23 (d, *J* = 5.1 Hz, 1H), 4.17 (d, *J* = 5.1 Hz, 1H), 2.41 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8, 141.5, 140.3, 131.9, 129.7, 129.4, 127.8, 125.9, 118.2, 115.2, 115.1, 114.7, 99.8, 81.0, 33.9, 31.3, 21.71, 21.67; HRMS *m/z* calculated for $[C_{22}H_{16}N_2Na]^+$ ($[M+Na]^+$): 331.1206, observed 331.1206; **(*trans*-8vf)**: yellow solid; m.p. 57 – 58 °C; ^{1}H NMR (400 MHz, $CDCl_3$); δ 7.61 (d, *J* = 8.1 Hz, 2H), 7.45 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 7.9 Hz, 2H), 4.11 (d, *J* = 2.4 Hz, 1H), 4.07 (d, *J* = 2.3 Hz, 1H), 2.41 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 141.6, 140.4, 131.9, 129.8, 129.4, 127.7, 125.9, 118.2, 115.92, 115.90, 114.7, 99.9, 80.9, 34.1, 31.4, 21.71, 21.67; HRMS *m/z* calculated for $[C_{22}H_{16}N_2Na]^+$ ($[M+Na]^+$): 331.1206, observed 331.1206.

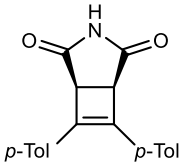
Methyl 4-(ethyl(*p*-tolyl)carbamoyl)-2,3-diphenylcyclobut-2-ene-1-carboxylate (8cg)



***cis*-8cg** ***trans*-8cg**

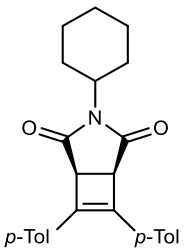
Prepared according to the ***General Procedure A*** using 1,2-diphenylethyne **6c** (0.1 mmol, 1.0 equiv.) and methyl (*Z*)-4-(ethyl(*p*-tolyl)amino)-4-oxobut-2-enoate **7g** (1.5 equiv.), 18 mg, 42% yield (*cis*/*trans* 1:5); white solid; (***cis*-8cg):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.49 (m, 2H), 7.41 – 7.38 (m, 2H), 7.31 – 7.22 (m, 10H), 4.07 – 4.02 (m, 2H), 3.86 (d, *J* = 5.5 Hz, 1H), 3.72 (s, 3H), 3.53 – 3.45 (m, 1H), 2.40 (s, 3H), 1.12 (t, *J* = 7.1 Hz, 3H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 169.3, 140.0, 139.7, 138.1, 138.0, 134.3, 134.2, 130.5, 128.5, 128.39, 128.35, 128.3, 128.2, 127.1, 126.8, 52.1, 46.9, 45.9, 44.7, 21.2, 13.1; HRMS *m/z* calculated for $[C_{28}H_{27}NNaO_3]^+$ ($[M+Na]^+$): 448.1883, observed : 448.1884; (***trans*-8cg):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.41 (m, 4H), 7.34 – 7.22 (m, 8H), 7.08 (d, *J* = 8.1 Hz, 2H), 3.95 (d, *J* = 2.0 Hz, 1H), 3.93 (d, *J* = 2.1 Hz, 1H), 3.83 (dq, *J* = 14.2, 7.1 Hz, 1H), 3.66 (dq, *J* = 14.2, 7.1 Hz, 1H), 3.50 (s, 3H), 2.39 (s, 3H), 1.10 (t, *J* = 7.1 Hz, 3H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 170.1, 140.4, 139.1, 138.2, 138.1, 134.2, 133.6, 130.4, 128.5, 128.44, 128.42, 128.38, 128.36, 126.8, 126.5, 51.9, 47.5, 45.1, 44.4, 21.2, 13.2; HRMS *m/z* calculated for $[C_{28}H_{27}NNaO_3]^+$ ($[M+Na]^+$): 448.1883, observed : 448.1885

6,7-di-*p*-tolyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8ah)



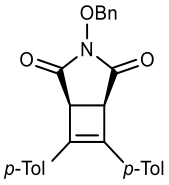
Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and maleimide **7h** (1.5 equiv.), 25 mg, 82% yield; white solid; m.p. 227 – 229 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.2 Hz, 4H), 7.58 (br s, 1H), 7.19 (d, *J* = 8.0 Hz, 4H), 4.08 (d, *J* = 1.0 Hz, 2H), 2.37 (s, 6H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4, 139.4, 138.1, 130.3, 129.5, 126.9, 46.4, 21.6; HRMS *m/z* calculated for $[C_{20}H_{18}NO_2]^+$ ($[M+H]^+$): 304.1332, observed : 304.1330

3-cyclohexyl-6,7-di-*p*-tolyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (**8ai**)



Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and 1-cyclohexyl-1*H*-pyrrole-2,5-dione **7i** (1.5 equiv.), 31 mg, 80% yield; white solid; m.p. 178 – 180 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.1 Hz, 4H), 7.17 (d, *J* = 8.0 Hz, 4H), 3.97 (s, 2H), 3.91 (tt, *J* = 12.3, 3.9 Hz, 1H), 2.36 (s, 6H), 2.15 – 2.00 (m, 2H), 1.85 – 1.75 (m, 2H), 1.68 – 1.56 (m, 2H), 1.36 – 1.11 (m, 4H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 139.2, 138.8, 130.5, 129.4, 126.9, 51.6, 44.6, 28.7, 26.0, 25.2, 21.6; HRMS *m/z* calculated for $[C_{26}H_{28}NO_2]^+$ ($[M+H]^+$): 386.2115, observed : 386.2115

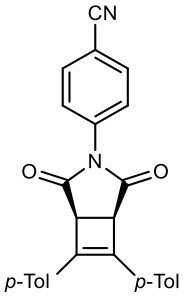
3-(benzyloxy)-6,7-di-*p*-tolyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (**8aj**)



Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and 1-(benzyloxy)-1*H*-pyrrole-2,5-dione **7j** (1.5 equiv.), 17 mg, 42% yield; white solid; m.p. 167 –

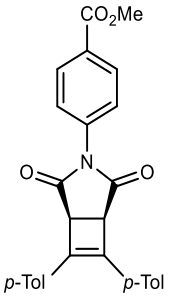
169 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.2 Hz, 4H), 7.39 – 7.36 (m, 2H), 7.21 – 7.17 (m, 7H), 5.07 (s, 2H), 3.97 (s, 2H), 2.38 (s, 6H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 139.5, 138.1, 133.3, 130.2, 130.1, 129.42, 129.36, 128.5, 126.9, 78.4, 42.2, 21.6; HRMS *m/z* calculated for $[C_{27}H_{23}NNaO_3]^+$ ($[M+Na]^+$): 432.1570, observed : 432.1583

4-(2,4-dioxo-6,7-di-*p*-tolyl-3-azabicyclo[3.2.0]hept-6-en-3-yl)benzonitrile (8ak)



Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and 4-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)benzonitrile **7k** (1.5 equiv.), 24 mg, 59% yield; white solid; m.p. 214 – 215 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.9 Hz, 2H), 7.67 (d, *J* = 8.2 Hz, 4H), 7.47 (d, *J* = 8.9 Hz, 2H), 7.20 (d, *J* = 7.9 Hz, 4H), 4.24 (s, 2H), 2.38 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 139.6, 138.1, 135.9, 129.9, 129.4, 127.0, 126.8, 118.1, 111.9, 44.8, 21.5; HRMS *m/z* calculated for $[C_{27}H_{21}N_2O_2]^+$ ($[M+H]^+$): 405.1598, observed : 405.1612

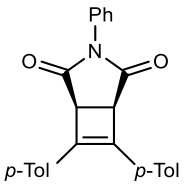
Methyl 4-(2,4-dioxo-6,7-di-*p*-tolyl-3-azabicyclo[3.2.0]hept-6-en-3-yl)benzoate (8al)



Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and methyl 4-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)benzoate **7l** (1.5 equiv.), 20 mg, 46% yield; white solid; m.p. 227 – 229 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.5 Hz, 2H), 7.68 (d, *J* = 8.3, 4H), 7.39 (d, *J* = 8.5 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 4H), 4.23 (s, 2H), 3.91 (s, 3H), 2.38 (s, 6H) ^{13}C NMR

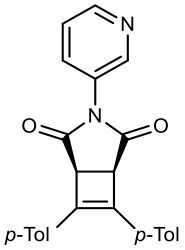
(100 MHz, $CDCl_3$) δ 173.7, 166.4, 139.6, 138.4, 136.2, 130.4, 130.2, 129.9, 129.5, 127.0, 126.5, 52.4, 45.0, 21.6; HRMS *m/z* calculated for $[C_{28}H_{24}NO_4]^+$ ($[M+H]^+$): 438.1700, observed : 438.1719

3-phenyl-6,7-di-*p*-tolyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8am)



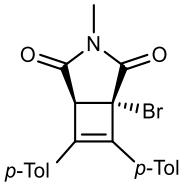
Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and 1-phenyl-1*H*-pyrrole-2,5-dione **7m** (1.5 equiv.), 11 mg, 29% yield; white solid; m.p. 185 – 187 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.1 Hz, 4H), 7.44 – 7.40 (m, 2H), 7.36 – 7.32 (m, 1H), 7.27 – 7.24 (m, 2H), 7.19 (d, *J* = 7.9 Hz, 4H), 4.21 (s, 2H), 2.37 (s, 6H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 139.5, 138.5, 132.1, 130.4, 129.5, 129.1, 128.6, 127.0, 126.7, 45.1, 21.6; HRMS *m/z* calculated for $[C_{26}H_{22}NO_2]^+$ ($[M+H]^+$): 380.1645, observed : 380.1645

3-(pyridin-3-yl)-6,7-di-*p*-tolyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8an)



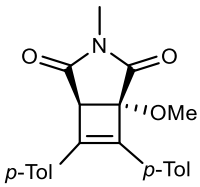
Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and 1-(pyridin-3-yl)-1*H*-pyrrole-2,5-dione **7n** (1.5 equiv.), 21 mg, 55% yield; white solid; m.p. 195 – 196 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 – 8.58 (m, 2H), 7.68 (d, *J* = 8.3 Hz, 4H), 7.66 – 7.63 (m, 1H), 7.36 (dd, *J* = 8.2, 4.8 Hz, 1H), 7.20 (d, *J* = 8.3 Hz, 4H), 4.25 (s, 2H), 2.38 (s, 6H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 149.3, 147.6, 139.7, 138.3, 134.0, 130.1, 129.5, 128.1, 127.0, 123.6, 45.1, 21.6; HRMS *m/z* calculated for $[C_{25}H_{21}N_2O_2]^+$ ($[M+H]^+$): 381.1598, observed : 381.1599

1-bromo-3-methyl-6,7-di-*p*-tolyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8ao)



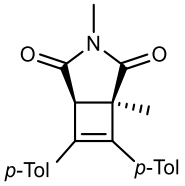
Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and 3-bromo-1-methyl-1*H*-pyrrole-2,5-dione **7o** (1.5 equiv.), 37 mg, 93% yield; pale yellow solid; m.p. 214 – 215 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.2 Hz, 2H), 7.63 (d, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 7.9 Hz, 2H), 4.30 (s, 1H), 3.01 (s, 3H), 2.40 (s, 3H), 2.37 (s, 3H) ^{13}C NMR (100 MHz, CD_2Cl_2) δ 172.9, 172.2, 141.4, 140.7, 138.9, 138.7, 130.00, 129.95, 129.4, 128.4, 128.2, 128.0, 56.0, 52.0, 25.8, 21.9, 21.8; HRMS *m/z* calculated for $[C_{21}H_{18}BrNNaO_2]^+$ ($[M+Na]^+$): 418.0413, observed : 418.0413

1-methoxy-3-methyl-6,7-di-*p*-tolyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8ap)



Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and 3-methoxy-1-methyl-1*H*-pyrrole-2,5-dione **7p** (1.5 equiv.), 34 mg, 98% yield; white solid; m.p. 152 – 154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.2 Hz, 2H), 7.66 (d, *J* = 8.2 Hz, 2H), 7.20 (d, *J* = 8.2 Hz, 4H), 4.11 (s, 1H), 3.42 (s, 3H), 2.99 (s, 3H), 2.37 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 173.5, 140.1, 139.4, 139.3, 138.7, 129.4, 129.4, 129.3, 128.9, 127.3, 127.1, 81.7, 53.4, 49.1, 24.7, 21.49, 21.48; HRMS *m/z* calculated for $[C_{22}H_{22}NO_3]^+$ ($[M+H]^+$): 348.1594, observed 348.1595.

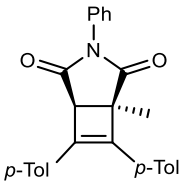
1,3-dimethyl-6,7-di-*p*-tolyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8aq)



Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and 1,3-dimethyl-1*H*-pyrrole-2,5-dione **7q** (1.5 equiv.), 29 mg, 88% yield; white solid; m.p. 182 –

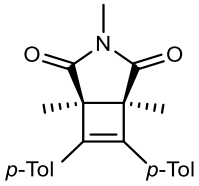
183 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.2 Hz, 2H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 7.16 (d, *J* = 7.9 Hz, 2H), 3.78 (s, 1H), 2.97 (s, 3H), 2.37 (s, 3H), 2.35 (s, 3H), 1.63 (s, 3H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.7, 175.0, 142.1, 139.3, 139.1, 137.2, 130.0, 129.9, 129.5, 129.4, 127.3, 126.9, 51.6, 50.9, 29.8, 25.0, 21.6, 15.8; HRMS *m/z* calculated for $[C_{22}H_{21}NNaO_2]^+$ ($[M+Na]^+$): 354.1465, observed : 354.1472.

1-methyl-3-phenyl-6,7-di-*p*-tolyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8ar)



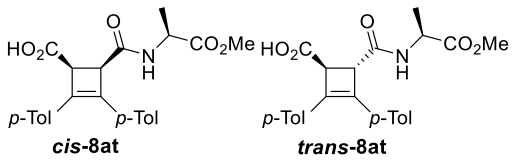
Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and 3-methyl-1-phenyl-1*H*-pyrrole-2,5-dione **7r** (1.5 equiv.), 39 mg, 99% yield; white solid; m.p. 210 – 211 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (t, *J* = 8.0 Hz, 4H), 7.47 – 7.31 (m, 3H), 7.27 (d, *J* = 8.6 Hz, 2H), 7.23 – 7.14 (m, 4H), 3.94 (s, 1H), 2.39 (s, 3H), 2.37 (s, 3H), 1.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4, 173.6, 142.1, 139.3, 139.0, 137.2, 132.1, 129.8, 129.7, 129.4, 129.3, 128.9, 128.3, 127.3, 126.9, 126.6, 51.3, 50.6, 21.48, 21.47, 15.8; HRMS *m/z* calculated for $[C_{27}H_{24}NO_2]^+$ ($[M+H]^+$): 394.1802, observed 394.1807.

1,3,5-trimethyl-6,7-di-*p*-tolyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8as)



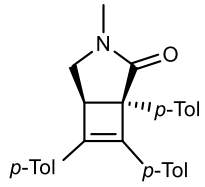
Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and 1,3,4-trimethyl-1*H*-pyrrole-2,5-dione **7s** (1.5 equiv.), 19 mg, 55% yield; white solid; m.p. 180 – 181 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.2 Hz, 4H), 7.14 (d, *J* = 7.9 Hz, 4H), 2.97 (s, 3H), 2.35 (s, 6H), 1.58 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.5, 142.1, 138.8, 129.7, 129.3, 127.2, 54.3, 24.8, 21.4, 13.3; HRMS *m/z* calculated for $[C_{23}H_{24}NO_2]^+$ ($[M+H]^+$): 346.1802, observed : 346.1808

4-(((*S*)-1-methoxy-1-oxopropan-2-yl)carbamoyl)-2,3-di-*p*-tolylcyclobut-2-ene-1-carboxylic acid (8at)



Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and (*S,Z*)-4-((1-methoxy-1-oxopropan-2-yl)amino)-4-oxobut-2-enoic acid **7t** (1.5 equiv.), 38 mg, 93% yield (*cis*/*trans* 4.4:1); The NMR spectrum was obtained on a partially purified material as a mixture of diastereomers; **(*cis*-8at) (d.r. 1:1) :** white solid; m.p. 168 – 169 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.63 (d, *J* = 6.9 Hz, 0.5H), 8.50 (d, *J* = 7.7 Hz, 0.5H), 7.44 – 7.27 (m, 4H), 7.19 – 7.10 (m, 4H), 4.29 (td, *J* = 7.3, 5.4 Hz, 1H), 4.11 – 4.01 (m, 2H), 3.61 (s, 1.5H), 3.59 (s, 1.5H), 2.29 (s, 3H), 2.28 (s, 3H), 1.29 (d, *J* = 7.3 Hz, 1.5H), 1.25 (d, *J* = 7.1 Hz, 1.5H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.5, 173.1, 171.8, 171.7, 170.1, 169.7, 138.4, 138.2, 138.12, 138.07, 137.8, 137.7, 137.6, 137.4, 131.92, 131.86, 131.60, 131.57, 129.5, 129.4, 129.22, 129.20, 127.2, 127.1, 126.48, 126.45, 52.3, 52.2, 48.11, 48.02, 47.97, 47.9, 45.5, 45.4, 21.4, 21.3, 17.8, 17.5.; HRMS m/z calculated for $[C_{24}H_{25}NNaO_5]^+$ ($[M+Na]^+$) : 430.1625, observed 430.1626; **(*trans*-8at) (d.r. 1.5:1)** : white solid; m.p. 190 – 192 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.75 (t, *J* = 8.7 Hz, 1H), 7.42-7.36 (m, 4H), 7.19 (t, *J* = 7.5 Hz, 4H), 4.29 (dp, *J* = 14.5, 7.2 Hz, 1H), 3.98 (d, *J* = 1.9 Hz, 0.6H), 3.91 (d, *J* = 1.8 Hz, 0.4H), 3.77 (d, *J* = 1.8 Hz, 0.6H), 3.72 (d, *J* = 1.8 Hz, 0.4H), 3.61 (s, 1.8H), 3.52 (s, 1.2H), 2.31 (s, 3.6H), 2.30 (s, 2.4H), 1.31 (d, *J* = 7.3 Hz, 1.2H), 1.24 (d, *J* = 7.2 Hz, 1.8H) ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.5, 173.4, 173.35, 173.26, 170.4, 170.3, 138.83, 138.80, 138.4, 138.33, 138.33, 138.30, 138.0, 137.9, 131.3, 131.15, 131.13, 131.13, 129.6, 129.6, 129.5, 129.4, 126.53, 126.49, 126.46, 126.4, 52.3, 52.2, 48.2, 48.0, 46.8, 46.7, 46.0, 45.6, 40.6, 21.39, 21.38, 17.6, 17.4; HRMS m/z calculated for $[C_{24}H_{25}NNaO_5]^+$ ($[M+Na]^+$) : 430.1625, observed 430.1625.

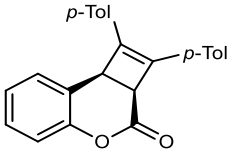
3-methyl-1,6,7-tri-*p*-tolyl-3-azabicyclo[3.2.0]hept-6-en-2-one (8av)



Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and 1-methyl-3-(p-tolyl)-1,5-dihydro-2H-pyrrol-2-one **7v** (1.5 equiv.), 17 mg, 43% yield; white solid;

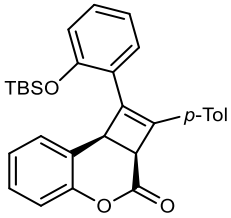
m.p. 170 – 171 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.2 Hz, 2H), 7.45 (d, *J* = 8.1 Hz, 2H), 7.20 (d, *J* = 8.1 Hz, 2H), 7.17 (d, *J* = 7.9 Hz, 2H), 7.08 – 7.05 (m, 4H), 3.60 (dd, *J* = 10.2, 8.2 Hz, 1H), 3.50 (dd, *J* = 8.2, 1.6 Hz, 1H), 3.30 (dd, *J* = 10.2, 1.7 Hz, 1H), 2.38 (s, 3H), 2.30 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 143.0, 139.8, 138.6, 138.1, 136.5, 135.5, 130.6, 130.5, 129.5, 129.3, 129.2, 127.8, 127.4, 126.9, 59.0, 48.4, 45.8, 30.8, 21.58, 21.57, 21.2; HRMS *m/z* calculated for $[C_{28}H_{28}NO]^+$ ($[M+H]^+$): 394.2165, observed : 394.2165.

1,2-di-*p*-tolyl-2a,8b-dihydro-3*H*-cyclobuta[*c*]chromen-3-one (**8aw**)



Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and coumarin **7w** (1.5 equiv.), 25 mg, 71% yield; white solid; m.p. 183 – 184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.23 – 7.18 (m, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 7.05 – 7.01 (m, 2H), 4.45 (d, *J* = 4.6 Hz, 1H), 4.35 (d, *J* = 4.6 Hz, 1H), 2.34 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 151.1, 144.2, 138.8, 138.6, 136.3, 131.2, 130.4, 129.4, 129.2, 129.1, 128.5, 127.4, 126.8, 124.4, 121.6, 117.6, 42.8, 41.8, 21.5; HRMS *m/z* calculated for $[C_{25}H_{21}O_2]^+$ ($[M+H]^+$): 353.1536, observed : 353.1538.

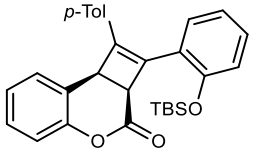
1-(2-((*tert*-butyldimethylsilyl)oxy)phenyl)-2-(*p*-tolyl)-2a,8b-dihydro-3*H*-cyclobuta[*c*]chromen-3-one (**8ww_a**)



Prepared according to the ***General Procedure A*** using *tert*-butyldimethyl(2-(*p*-tolylethynyl)phenoxy)silane **6w** (0.1 mmol, 1.0 equiv.) and coumarin **7w** (1.5 equiv.), 27 mg, 58% yield; white solid; m.p. 51 – 52 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.2 Hz, 2H), 7.23 – 7.13 (m, 3H), 7.08 – 7.06 (m, 2H), 7.03 – 7.01 (m, 2H), 6.96 – 6.87 (m, 3H), 4.59 (d, *J* = 4.6 Hz, 1H), 4.38 (d, *J* = 4.6 Hz, 1H), 2.31 (s, 3H), 0.80 (s, 9H), 0.09 (s, 3H), -0.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 153.6, 150.7, 142.4, 138.5, 137.2, 130.8, 130.1, 129.7, 129.0, 128.4, 128.2, 126.8, 125.9, 124.5,

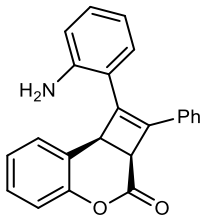
121.7, 121.4, 120.3, 117.3, 42.6, 42.1, 25.7, 21.5, 18.2, -4.0, -4.6; HRMS *m/z* calculated for $[C_{30}H_{33}O_3Si]^+$ ($[M+H]^+$): 469.2193, observed : 469.2193.

2-(2-((*tert*-butyldimethylsilyl)oxy)phenyl)-1-(*p*-tolyl)-2a,8b-dihydro-3*H*-cyclobuta[*c*]chromen-3-one (8ww_b)



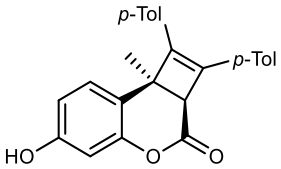
Prepared according to the ***General Procedure A*** using *tert*-butyldimethyl(2-(*p*-tolylethynyl)phenoxy)silane **6w** (0.1 mmol, 1.0 equiv.) and coumarin **7w** (1.5 equiv.), 15 mg, 32% yield; white solid; m.p. 148 – 149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.33 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.25 – 7.20 (m, 2H), 7.13 (td, *J* = 7.5, 1.3 Hz, 1H), 7.06 – 7.03 (m, 3H), 6.98 (td, *J* = 7.5, 1.1 Hz, 1H), 6.87 (dd, *J* = 8.3, 1.1 Hz, 1H), 4.51 (d, *J* = 4.5 Hz, 1H), 4.39 (d, *J* = 4.5 Hz, 1H), 2.28 (s, 3H), 0.74 (s, 9H), 0.09 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 153.8, 151.6, 145.7, 138.5, 135.2, 131.1, 130.3, 129.83, 129.79, 129.0, 128.6, 126.9, 125.4, 124.4, 122.0, 121.3, 119.8, 118.0, 44.6, 41.3, 25.6, 21.5, 18.2, -4.0, -4.5; HRMS *m/z* calculated for $[C_{30}H_{33}O_3Si]^+$ ($[M+H]^+$): 469.2193, observed : 469.2193.

1-(2-aminophenyl)-2-phenyl-2a,8b-dihydro-3*H*-cyclobuta[*c*]chromen-3-one (8xw)



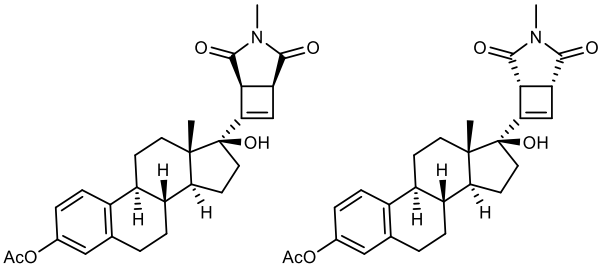
Prepared according to the ***General Procedure A*** using 2-(phenylethynyl)aniline **6x** (0.1 mmol, 1.0 equiv.) and coumarin **7w** (1.5 equiv.), 23 mg, 68% yield; white solid; m.p. 88 – 89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.59 (m, 2H), 7.34 – 7.28 (m, 3H), 7.23 – 7.19 (m, 1H), 7.17 – 7.13 (m, 1H), 7.10 – 7.04 (m, 3H), 7.03 – 6.99 (m, 1H), 6.75 (td, *J* = 7.5, 1.1 Hz, 1H), 6.68 (dd, *J* = 8.1, 1.1 Hz, 1H), 4.52 (d, *J* = 4.7 Hz, 1H), 4.50 (d, *J* = 4.6 Hz, 1H), 3.66 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 150.7, 143.9, 142.9, 137.9, 132.9, 129.8, 128.9, 128.8, 128.8, 128.6, 128.5, 127.1, 124.6, 121.2, 119.3, 118.1, 117.5, 115.8, 42.6, 42.5; HRMS *m/z* calculated for $[C_{23}H_{18}NO_2]^+$ ($[M+H]^+$): 340.1332, observed : 340.1331.

6-hydroxy-8b-methyl-1,2-di-*p*-tolyl-2a,8b-dihydro-3*H*-cyclobuta[*c*]chromen-3-one (8ax)



Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **6a** (0.1 mmol, 1.0 equiv.) and 4-methylumbelliferone **7x** (1.5 equiv.), 29 mg, 76% yield; white solid; m.p. 236 – 237 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.2 Hz, 2H), 7.15 – 7.06 (m, 7H), 6.70 (d, *J* = 2.5 Hz, 1H), 6.61 (dd, *J* = 8.5, 2.6 Hz, 1H), 3.98 (s, 1H), 2.36 (s, 3H), 2.30 (s, 3H), 1.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 156.0, 150.7, 149.0, 138.6, 138.4, 134.7, 131.0, 130.1, 129.4, 129.2, 128.2, 127.5, 126.7, 117.8, 112.1, 104.6, 50.4, 46.3, 24.1, 21.55, 21.52; HRMS *m/z* calculated for $[C_{26}H_{23}O_3]^+$ ($[M+H]^+$): 383.1642, observed : 383.1644.

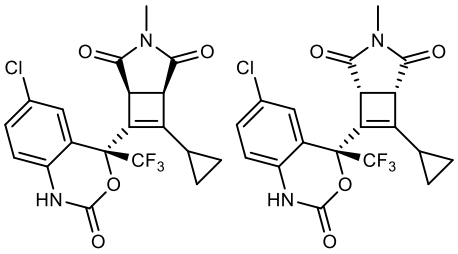
(8*R*,9*S*,13*S*,14*S*,17*S*)-17-hydroxy-13-methyl-17-(3-methyl-2,4-dioxo-3-azabicyclo[3.2.0]hept-6-en-6-yl)-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl acetate (8ya)



Prepared according to the ***General Procedure A*** using 17α-ethynylestradiol 3-acetate **6y** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (1.5 equiv.), 30 mg, 66% yield (d.r. 1.4:1); yellow viscous oil; The NMR spectrum was obtained on a partially purified material as a mixture of diastereomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (t, *J* = 7.7 Hz, 1H), 6.83 (d, *J* = 8.5 Hz, 1H), 6.79 (s, 0.6H), 6.79 (s, 0.4H), 6.19 (d, *J* = 1.0 Hz, 0.6H), 6.18 (d, *J* = 1.0 Hz, 0.4H), 3.98 (d, *J* = 3.2 Hz, 0.4H), 3.87 (d, *J* = 3.2 Hz, 0.6H), 3.73 (dd, *J* = 3.2, 0.9 Hz, 0.6H), 3.65 (dd, *J* = 3.2, 0.9 Hz, 0.4H), 2.99 (s, 1.8H), 2.98 (s, 1.2H), 2.91 – 2.82 (m, 2H), 2.72 (s, 0.4H), 2.49 (s, 0.6H), 2.38 – 2.20 (m, 4H), 2.22 – 2.09 (m, 2H), 2.05 – 1.82 (m, 4H), 1.64 – 1.46 (m, 5H), 1.42 – 1.27 (m, 3H), 0.95 (s, 1.8H), 0.92 (s, 1.2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.05, 175.08, 175.07, 174.8, 169.83, 169.80, 158.7, 157.4, 148.46, 148.46, 138.14, 138.14, 137.6, 137.5, 130.4, 128.5, 126.25, 126.25, 121.52, 121.51, 118.59, 118.58, 84.2, 84.0, 49.7, 48.9, 48.8, 47.75, 47.70, 43.68, 43.65, 42.74, 42.66, 41.4, 39.0, 38.9, 37.5, 36.4, 33.5, 32.0, 29.5, 29.4,

28.2, 27.2, 27.2, 26.1, 26.0, 25.1, 24.8, 23.2, 23.1, 21.1, 14.1, 13.6.; HRMS m/z calculated for $[C_{27}H_{32}NO_5]^+$ ([M+H$^+$): 450.2275, observed 450.2275.

6-(6-chloro-2-oxo-4-(trifluoromethyl)-1,4-dihydro-2*H*-benzo[*d*][1,3]oxazin-4-yl)-7-cyclopropyl-3-methyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (8za)



Prepared according to the ***General Procedure A*** using Efavirenz **6z** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **7a** (15.0 equiv.), 19 mg, 45% yield (d.r. = 2.3:1); yellow viscous oil; The NMR spectrum was obtained on a partially purified material as a mixture of diastereomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.28 (s, 1H), 7.39 – 7.35 (m, 1.3H), 7.34 (d, *J* = 2.2 Hz, 0.3H), 7.29 (s, 0.3H), 6.89 (dd, *J* = 8.5, 1.3 Hz, 0.3H), 6.85 (d, *J* = 8.4 Hz, 0.7H), 3.69 (d, *J* = 3.4 Hz, 0.7H), 3.56 (d, *J* = 3.5 Hz, 0.3H), 3.48 (d, *J* = 3.4 Hz, 0.3H), 3.45 (d, *J* = 3.4 Hz, 0.7H), 2.92 (s, 0.9H), 2.90 (s, 2.1H), 1.82 – 1.66 (m, 2H), 1.34 – 1.20 (m, 1H), 1.05 – 0.80 (m, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) 173.6, 173.2, 173.2, 173.0, 155.3, 154.3, 148.5, 148.3, 134.1, 133.9, 131.6, 131.5, 130.9, 130.4, 129.2, 128.9, 126.8, 126.6, 116.7, 116.6, 114.1, 114.0, 77.3, 77.2, 43.7, 43.6, 43.0, 42.9, 25.1, 24.9, 10.8, 10.6, 7.9, 7.6, 7.0, 6.9.; HRMS *m/z* calculated for $[C_{19}H_{14}ClF_3N_2NaO_4]^+$ ([M+Na]$^+$): 449.0486, observed 449.0485.

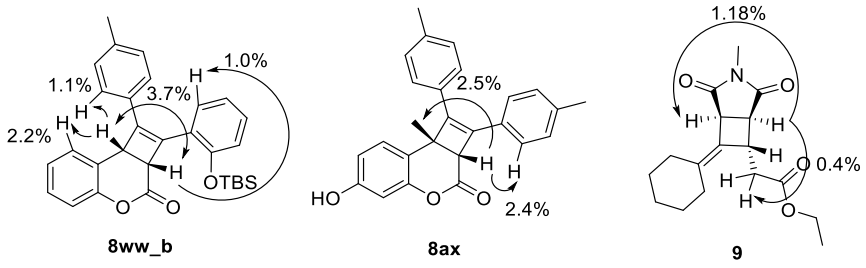


Figure 2-8. Stereochemical assignments by 1D NOE experiments

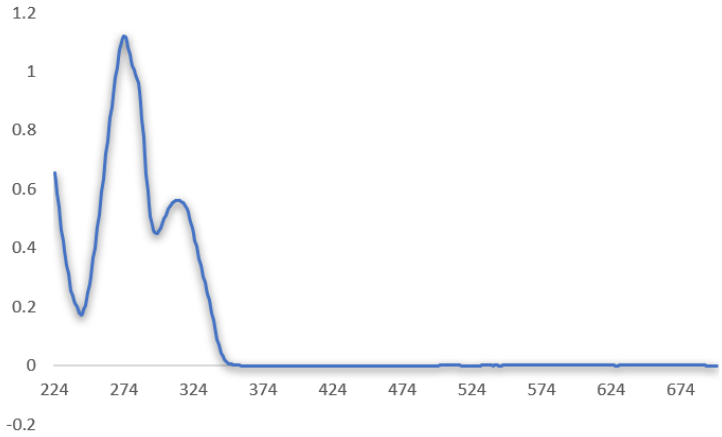


Figure 2-9. UV-Vis absorption spectrum data of 7w

Chapter 3.

Visible Light-promoted Enyne Photometathesis via Tandem Energy Transfer

3.1. Ring Closing Enyne Metathesis

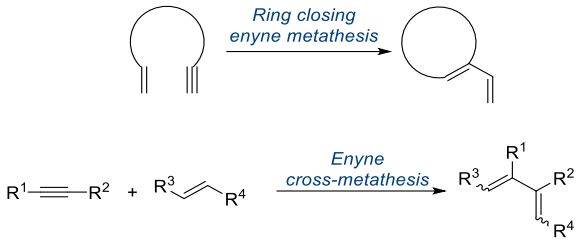
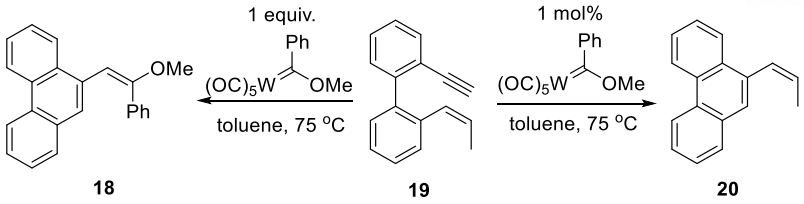


Figure 3-1. Enyne metathesis

Enyne metathesis is a variation of olefin metathesis reaction occur between alkenes and alkynes with a metal carbenoid complex as a catalyst producing a butadiene (Figure 3-1). In other sentence, it contains the combination of alkenes and alkynes to afford a corresponding 1,3-diene. Enyne metathesis is a powerful approach for the synthesis of highly stereoselective 1,3-diene systems under mild conditions by employing simpler substrate. The fact that not only to being a means to an end in itself, but also the 1,3-diene so formed are themselves various synthetic intermediates that can proceed further selective transformations enhances the synthetic value of this reaction. In addition, enyne metathesis can give complete atom economy, that possesses olefin-side-product is not produced upon reaction. It means that the reaction is driven by enthalpic factors, the stability of the 1,3-diene so produced principally. Also, any several independent mechanisms can achieve enyne metathesis during the process of the reaction. Even if the net result is identical usually, the reaction is dictated by whether the transition metal complex or metal carbene species operate the process. The ring closing enyne metathesis is an intramolecular version, which is an efficient method for the formation of both heterocyclic and carbocyclic ring. In 1985, Katz group developed enyne metathesis of diphenyl enyne to afford phenanthrene at the first (Scheme 3-1).[45] Phenanthrene **18** can be prepared when using the carbene, which is a tungsten carbonyl group, in the reaction as stoichiometric amounts. And phenanthrene **20** can be obtained when using as catalytic amounts. When a metal atom is solely added on to alkyne carbon initially during the reaction, the reaction stereoselectivity is great when a metal atom is solely added on to alkyne carbon.

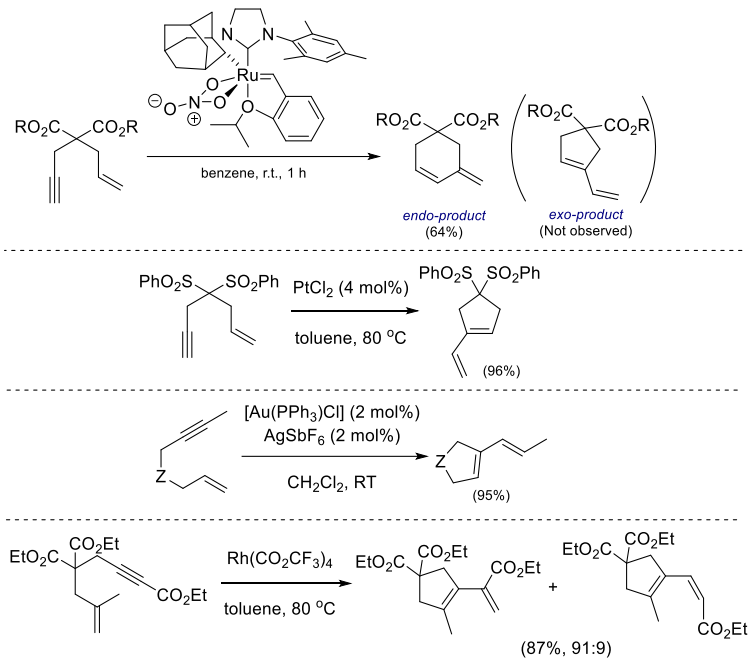


Scheme 3-1. First enyne metathesis by Katz et al.

Mori et al. found out that Grubbs catalyst is effective for enyne metathesis in 1994.[46] They demonstrated its applicability to the formation of five-, six-, and seven-membered nitrogen-containing heterocyclic rings. Inspired by this achievement, there are many approaches discovered for synthesis of 1,3-diene using Ru catalysts. It is well-known that Ru-based Grubbs catalysts undergo a highly selective α-addition to alkynes to promote exo-cyclization during ring-closing enyne metathesis or to produce conjugated polyenes containing five-membered rings during the cyclopolymerization of 1,6-heptadiynes. In 2016, Choi group reported the first example of *β*-selective addition to alkynes using Grubbs Z-selective catalyst, which produces only endo products during the ring-closing enyne metathesis reaction of terminal enynes and promoted the cyclopolymerization of 1,6-heptadiyne derivatives to give conjugated polyenes containing a six-membered ring as a major repeat unit (Scheme 3-2).[47] Not only Ru catalysts but also various transition metal catalysts have been utilized for ring closing enyne metathesis. $PtCl_2$ also constituted an efficient and practical catalyst for ring closing enyne metathesis producing conjugated diene.[48] In addition, the method includes a set of different rearrangement of enyne with atom economy. If not-saturated ethers are used, they accomplished the synthesis for polycycles bearing cyclopropane and also unexpected O – C allyl migration. Echavarren et al. reported theoretical and experimental studies that enlighten the complicated mechanistic problems using gold catalyst.[49] This work strongly suggests that cyclobutene intermediates are not necessary in the skeletal rearrangement of enynes. Chatani group demonstrated that Rh(II) complexes are also active in the skeletal reorganization of 1,6- and 1,7-enynes to 1-vinylcycloalkenes.[50] A characteristic feature of the Rh(II)-catalyzed skeletal reorganization of enynes is the wide applicability of enynes having a substituent, such as an alkyl, aryl, chloro, and ester substituent at the alkyne carbon. Most importantly, two possible isomers of 1-vinylcycloalkenes can be obtained, the ratio of which are significantly depending on the pattern of substituents of the enynes.

The reaction mechanism of ring closing enyne metathesis can be classified by two pathways (Figure 3-2). Exo- and endo-pathway can decide the structure depending on which carbon of alkyne metal catalyst binds with. If the metal coordinates selectively to the alkyne **21** in exo-pathway, cyclopropyl-metal

carbenes **22** are initially formed, which can react with alcohols or water to give products of alkoxy- or hydroxycyclization, whereas in the absence of nucleophiles, skeletal rearrangement forms dienes **23**



Scheme 3-2. Transition metal-catalyzed enyne metathesis

and/or **24**. Alternatively, coordination of MX_n to the alkyne and the alkene is followed by oxidative cyclometallation to form 5-membered bicyclic intermediate **26**, which usually evolves by β-hydrogen elimination to give Alder-ene-type products. Formation of products **23** could also occur by conrotatory ring-opening of cyclobutenes **27**, which are formed either from **22** or by reductive elimination of **26**. A

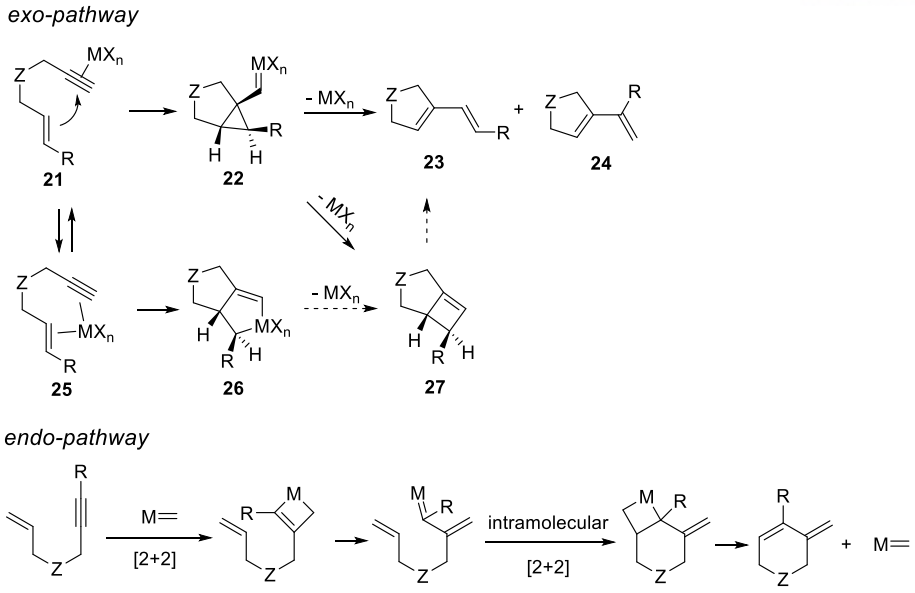
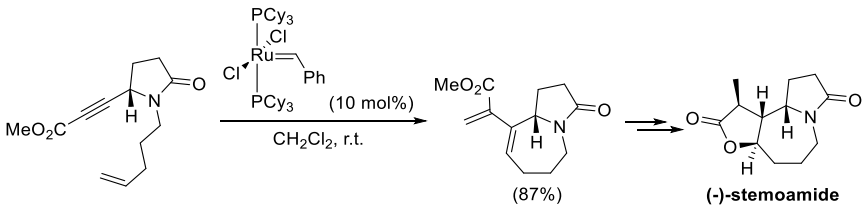
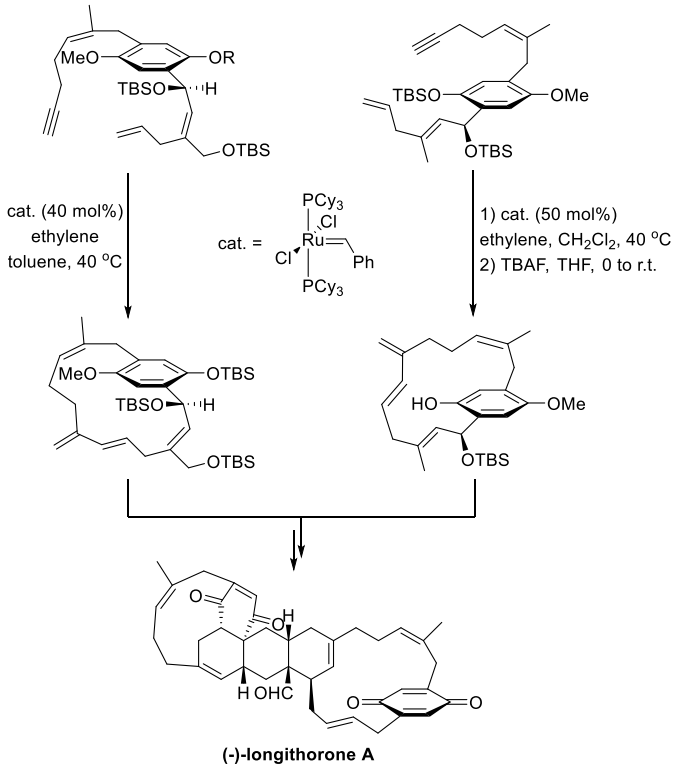


Figure 3-2. General pathways of ring closing enyne metathesis

pathway for the formation of **23** via ring-opening of **27** is favored by most chemists. However, the formation of dienes **24** requires a different mechanistic rationalization. Because ring closing enyne metathesis is useful method for the formation of cyclic compounds, it has been well utilized in total synthesis.[51] Several stylish and informative applications of the enyne metathesis. Mori group has developed the ruthenium carbenoid catalyzed enyne metathesis. They reported the first total synthesis, which achieved an enyne metathesis for the synthesis of tricyclic alkaloid (-)-stemoamide in 1996 (Scheme 3-3).[52] This reaction is even more remarkable comparing to previous work by chemists on the ring closing enyne metathesis of alkyne moieties with carboalkoxy groups.



Scheme 3-3. Total synthesis of (-)-stemoamide

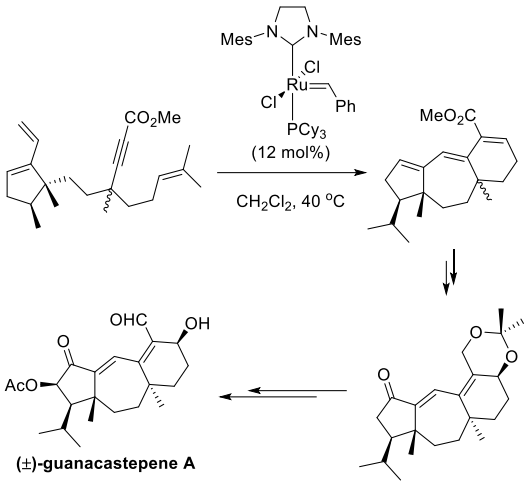


Scheme 3-4. Total synthesis of (-)-longithorone A

In other words, the intramolecular cyclization is promoted by the ester group, while the obtained unstable cross-conjugated compound generally proceeds further decomposition during isolation and is separated only in low yields. To account for the obvious discrepancy in the outstanding consequence, it was suggested that the conjugated diene is compelled to take up on a non-planar form in which the junction between the alkene π-systems is reduced by a steric hindrance, thus defending the system from destruction expected to occur in other ways. A few more steps were needed to synthesize target-product after enyne metathesis. The regiochemical result of macrocyclizations using enyne metathesis surely promoted for Shair et al. to attain the synthesis for (-)-longithorone A (Scheme 3-4).[53] Enyne metathesis applied to the macrocycle formation at the first time, which had usually afforded the 1,2-disubstituted cycloadduct. They suggested to use an elegant sequence of both intra- and intermolecular Diels-Alder reactions to construct these noteworthy natural products.

The enyne metathesis can be well established for cascade reactions to afford polycycles from simple substrates. A ring closing enyne metathesis first provides a fresh metal carbenoid which can be possibly blocked by another properly sited alkene in the same compound, achieving a next enyne metathesis to synthesize another a fresh metal carbenoid and ring moieties, etc. In 2004, the Hanna group reported an

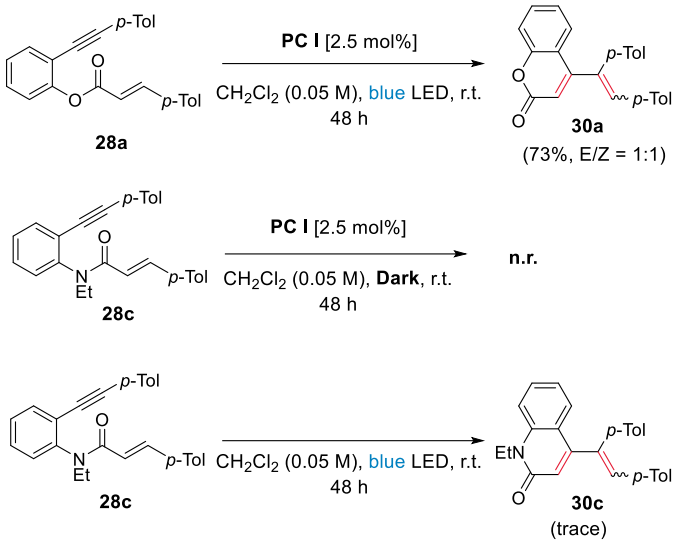
cascade ring closing enyne metathesis in the total synthesis of guanacastepene A (Scheme 3-5).[54]



Scheme 3-5. Total synthesis of guanacastepene A

3.2. Design of Enyne photometathesis

A good achievement of intra-cycloaddition of alkene with alkyne can give an approach for important cyclo-products. The enyne **28a** tethered by ester group was transformed to the unexpected product, which was turned to be coumarin **30a** in 73% yield (E/Z = 1:1; Scheme 3-6) at standard condition. We guessed that the formation of 1,3-diene was caused by electrocyclic ring opening of the cyclobutene initially formed. In addition, Without light or catalyst, there was no reaction as the control experiments. Therefore, the photo-promoted intramolecular cycloaddition of enyne gives an accessibility for the conjugated dienes with high substitution despite employing simpler substrates. This synthetic route can provide complementary methods for the *ring closing enyne metathesis*.



Scheme 3-6. Enyne photometathesis and control experiments

Therefore, we developed a new synthetic approach of the synthesis of conjugated dienes through triplet tandem excitation obtaining cyclobutene products (Figure 3-3). Prepared enynes can be converted to 1,3-dienes bearing pharmacological active molecules such as coumarin and 2-quinolone derivatives. Interestingly, only limited number of examples for the formation of conjugated dienes with high substitution via enyne metathesis have been known to date. As such, we were prompted to perform a comparison by using **28a**. While our synthetic method afforded 1,3-diene **30a** in 73% yield, Ru-catalyzed ring closing enyne metathesis failed to attain **30a** (Scheme 3-7).

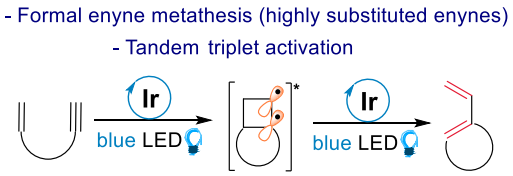
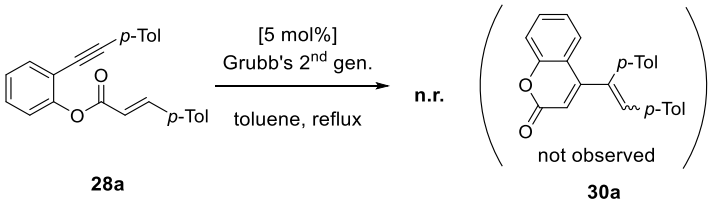


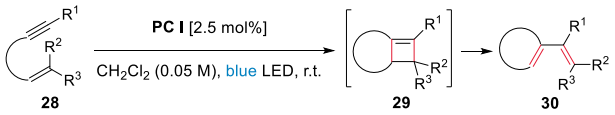
Figure 3-3. Enyne photometathesis under visible light

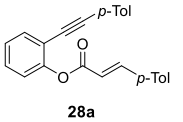
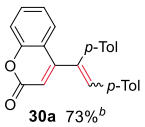
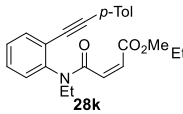
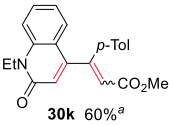
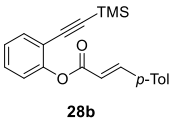
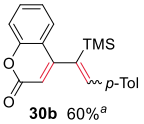
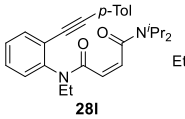
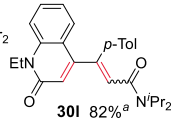
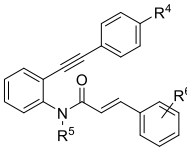
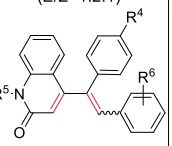
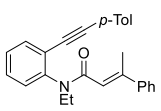
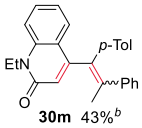
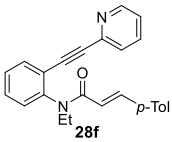
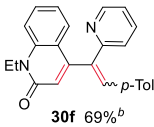
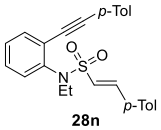
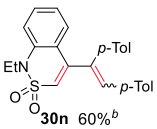
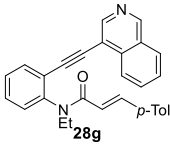
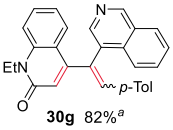
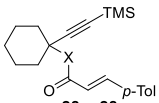
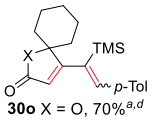
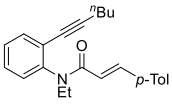
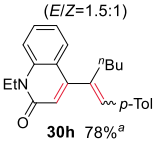
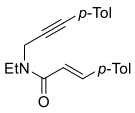
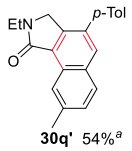
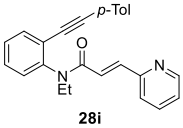
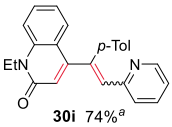
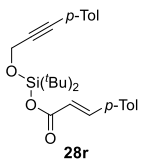
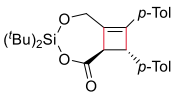
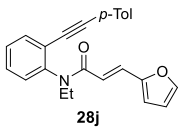
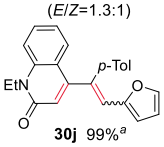


Scheme 3-7. Comparison with Ru-catalyzed ring closing enyne metathesis

3.3. Substrate Scope for Enyne Photometathesis

Table 3-1. Substrate scope of enyne photometathesis



Substrate	Product	Substrate	Product
 **28a**	 **30a** 73%[b] (*E*/*Z*=1:1)	 **28k**	 **30k** 60%[a] (*E*/*Z*=1.5:1)
 **28b**	 **30b** 60%[a] (*E*/*Z*=1.2:1)	 **28l**	 **30l** 82%[a] (*E*/*Z*=1:2.4)
 **28c**, **28d**, **28e**	 **30c** R^4 = Me, R^5 = Et, R^6 = 4-Me 80%[a] (*E*/*Z*=2:1) **30d** R^4 = H, R^5 = Et, R^6 = 2-Br 74%[b] (*E*/*Z*=1.8:1) **30e** R^4 = Me, R^5 = Ph, R^6 = 4-Me 95%[a] (*E*/*Z*=1.5:1)	 **28m**	 **30m** 43%[b] (*E*/*Z*=1.2:1)
 **28f**	 **30f** 69%[b] (*E*/*Z*=1:2.8)	 **28n**	 **30n** 60%[b] (*E*/*Z*=1.3:1)
 **28g**	 **30g** 82%[a] (*E*/*Z*=1.5:1)	 **28o**, **28p**	 **30o** X = O, 70%[a,d] (*E*/*Z*=1:1) **30p** X = NPh, 60%[b] (only *Z*)
 **28h**	 **30h** 78%[a] (*E*/*Z*=1.7:1)	 **28q**	 **30q'** 54%[a]
 **28i**	 **30i** 74%[a] (*E*/*Z*=1.3:1)	 **28r**	 **29r** 62%[c]
 **28j**	 **30j** 99%[a] (*E*/*Z*=1.2:1)		

Unless other noticed, the intramolecular reactions were proceeded under blue light from 12 W LED strip and argon gas with 0.1 mmol scale; Isolated by column chromatography. [a] Reaction time : 1 – 18 h [b] Reaction time : 24 – 48 h [c] **29r** is racemic, reaction time : 60 h. [d] It was performed using 0.05 mmol scale; The concentration of reaction was 0.01 M.

We examined the scope of the alkyne moiety to see that it has wide tolerability (Table 3-1). The substitution with *p*-tolyl and TMS functional groups afforded the corresponding 1,3-diene in good yields (**30a** and **30b**). The substitution ester to amido tethers could be transformed to corresponding 2-quinolones **30c - 30e** in good to excellent yields. A variety type of substitution with aryl/heteroaryl and alkyl functional groups showed good tolerability for affording desired 2-quinolone derivatives. For instance, 2-quinolones **30f** and **30g** with heteroaryl groups were easily synthesized by using pyridine and isoquinoline substituted alkynes, respectively. Moreover, changes of the alkene part to a variety of groups containing pyridine, furan, ester, and amide gave desired product in good to outstanding yields (**30i** – **30l**). The steric effect of alkene part was investigated with the enyne **28m** containing a highly substituted alkene, which afforded 1,3-diene **30m** in moderate yield. Besides amido tethers, an enyne with sulfonamide tether can be also transformed to be corresponding sultam **30n**. Finally, we investigated the probability of the formation of spiro-cycles from the enynes with ester and amido-tethers, which well afforded the corresponding conjugated dienes **30o** and **30p**, respectively. Surprisingly, the reaction of enyne **28q** furnished **30q'** through electrocyclization of the initially formed diene as an intermediate. Furthermore, the reaction of enyne **28r** with silyl tether gave unique cyclobutene product **29r**, which is fused with 7-membered ring in 62% yield. However, other trials were failed to afford 1,3-dienes from enynes shown in Figure 3-4. Enynes **31** and **32** including less-activated alkene couldn't give desired 1,3-dienes. While silyl-tethered enyne succeeded to transform to 7-membered ring fused cyclobutene, Enyne **33** underwent only E/Z isomerization of alkene part without transforming to desired product. The intramolecular reaction of enyne **28s** bearing benzofuran as alkene part afforded an unexpected product, which was turned out to be **29s'** in 74% (Scheme 3-8). It is in contrast to the synthesis of 1,3-diene using other intramolecular enynes without heterocyclic substituent groups, which occurs via ring opening of cyclobutenes. This unique product would be obtained because of activation of the cyclobutene **29s** provides 1,2-diradical **34**, that fragmented to afford 1,5-diradical **35** and then undergoes recombination to attain **29s'**. This rearrangement can be also performed using enyne bearing benzothiophene **28t** and **28u** to give **29t'** and **29u'** in excellent yields. To see whether ring expansion can occur, **29t'** was heated up to 100 °C. To our satisfaction, polycyclic product **30t'** was given to 65% yield, that would be explained through sulfur extrusion after ring-opening of 4-membered ring. In addition, the polycycle formation from **29u'** well achieved to afford the rearranged adduct **30u'** in 86% yield.

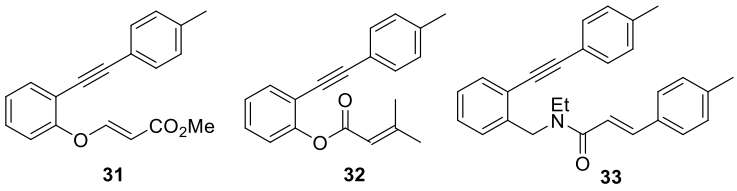
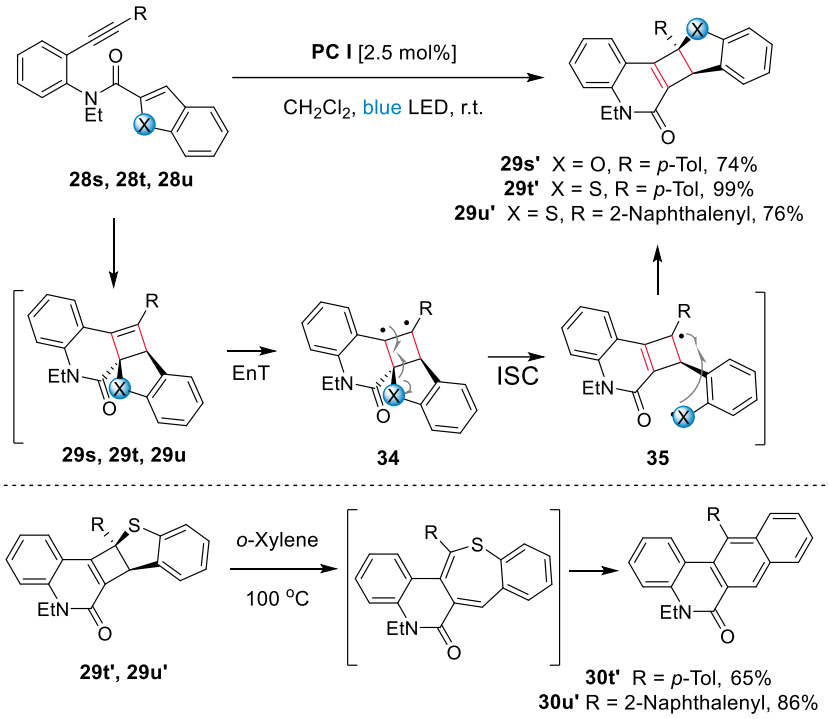
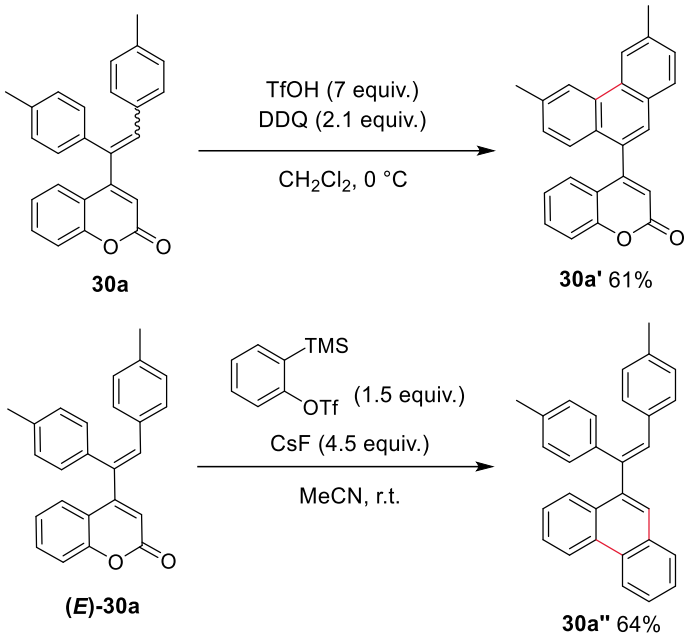


Figure 3-4. Scope of failed enynes



Scheme 3-8. Rearrangement of benzofuran and benzothiophene

3.4. Transformation of 1,3-Dienes to Phenanthrenes

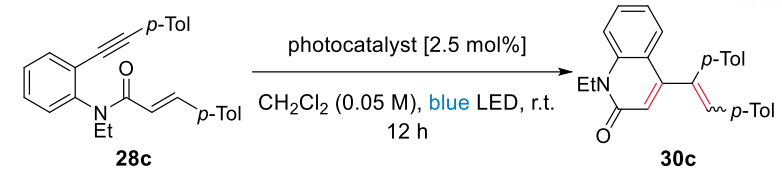


Scheme 3-9. Application for extended π-system compounds

Extended π-system is a valuable aspect in a variety of applications such as material science and fluorescence sensors.[55-58] Therefore, we examined the accessibility for such compounds using our synthetic approach (Scheme 3-9). Moreover, we proved that each phenanthrene **30a'** and **30a''** could be easily synthesized using 1,3-diene **30a** by oxidative electro-cyclization and benzyne [4+2] cycloaddition.

3.5. Proposed Mechanism of Enyne Photometathesis

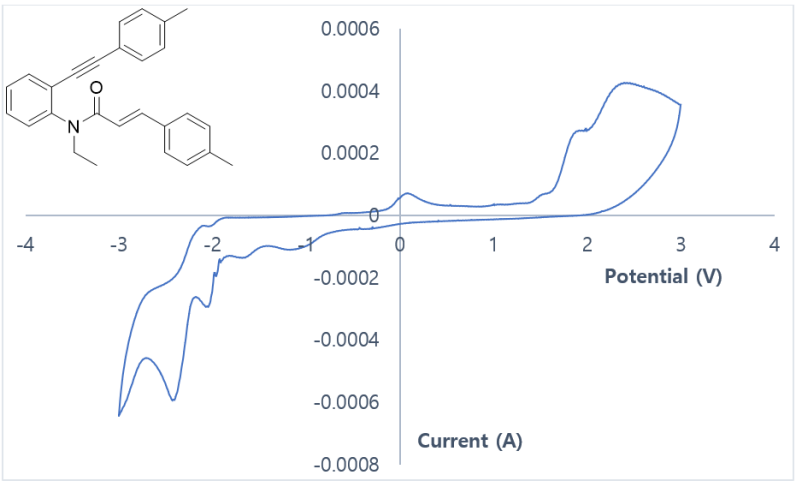
To investigate whether triplet energy transfer is also operative in the intramolecular reaction, we compared with among selected photocatalysts (Scheme 3-10). First, we chosed **PC II** and **VI** because the triplet energy level of **28c** (49.0 kcal/mol) is similar or lower than their triplet energy levels. Ruthenium catalyst and organic dye, which are shown and have lower triplet energy levels, were also chosen as a control. The outcomes were shown in Figure 47, which had a good agreement with triplet energy levels of photocatalysts. Furthermore, it's remarkable in that photocatalyst **PC VI** afforded **30c** in 67% while it was ineffective for the intermolecular cycloaddition because it had lower triplet energy than that of maleimide (55.9 kcal/mol).



PC II	PC VI	$Ru(bpy)_3(PF_6)_2$	Eosin Y[a]
67%	67%	4%	n.r.

Scheme 3-10. Screening of catalysts for enyne photometathesis

In addition, we examined the reduction and oxidation potential of **28c** using cyclic voltammogram, the reduction potential ($E_{p/2}^{red}$ = -2.13 and -2.44 V vs SCE) seemed to be insufficient to attain reduction by the photocatalysts (Figure 3-5). This result proposed that the mechanism of intramolecular reaction would be triplet energy transfer.



$E_{p/2}^{ox}$ = +1.82, +0.11 V vs SCE, $E_{p/2}^{red}$ = -2.13, -2.44 V vs SCE

Figure 3-5. Cyclic voltammetry of enyne 28c

The result of Stern-Volmer quenching experiment using enyne **28c** also showed the same trend with several catalysts (Figure 3-6). The degree of catalyst quenching by **28c** was consistent with their triplet energy levels, while it was inconsistent with their redox potentials. The most noticeable quenching was observed using **PC I** with the highest triplet energy. These results show that the reaction is proceeded through triplet energy transfer.

Photocatalyst (0.1 mM)		Quencher : 4c					
Cat.	Max emission wavelength	0 mM	2 mM	4 mM	6 mM	8 mM	10 mM
PC I	472 nm	1	5.0653	10.3184	17.0076	22.4114	33.8915
PC IV	505 nm	1	1.6578	2.8213	4.2890	5.2490	5.9022
PC V	527 nm	1	1.2920	1.5187	1.6922	1.9659	2.2069
PC VI	562 nm	1	1.0597	1.1066	1.1730	1.2388	1.3084

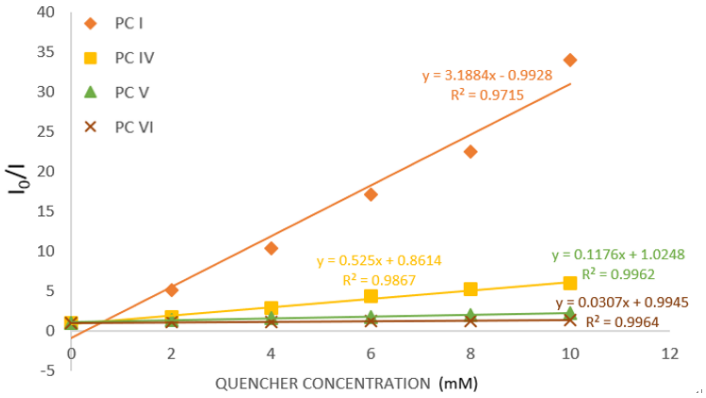


Figure 3-6. Stern-Volmer plot using 28c as a quencher

To figure out whether a radical chain mechanism is in operation for the reaction, we performed light on-off experiments for intramolecular reaction of enyne **28d** (Figure 3-7). The reaction stopped without light like the intermolecular cycloaddition, which excludes the radical chain process.

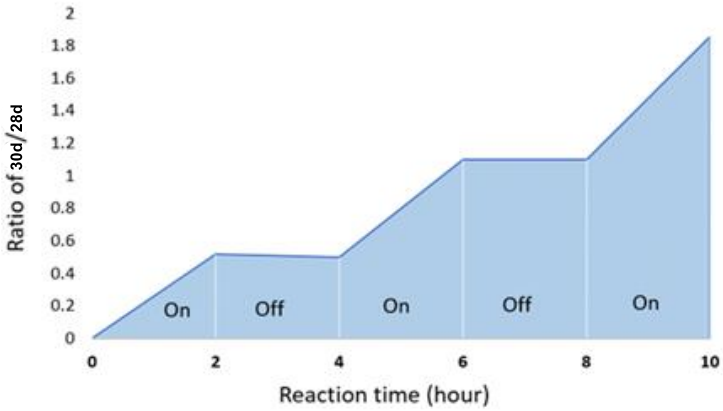


Figure 3-7. Light on-off experiment of enyne photometathesis

In our hypothesis, triplet tandem excitation of initially formed cyclobutene derivatives might lead to formation of conjugated dienes (Figure 3-8). After further mechanism study such as DFT calculations, it was found that the cyclobutene **29c** could be easily activated to the triplet state (41.2 kcal/mol) by that of photocatalyst **PC I** (60.8 kcal/mol). In summary, enyne **28c** would be excited to its triplet state in photocatalysis to afford diradical intermediate **28c*** and undergoes radical addition on alkyne moiety to be transformed to be **Int-29c**, which converts to **29c** after inter system crossing process. Cyclobutene **29c** excited to its triplet state by Ir photocatalyst to attain diradical intermediate **29c***, which can have isomerization to afford **Int-30c**. It may undergo inter system crossing process to be transformed to 1,3-diene **30c**.

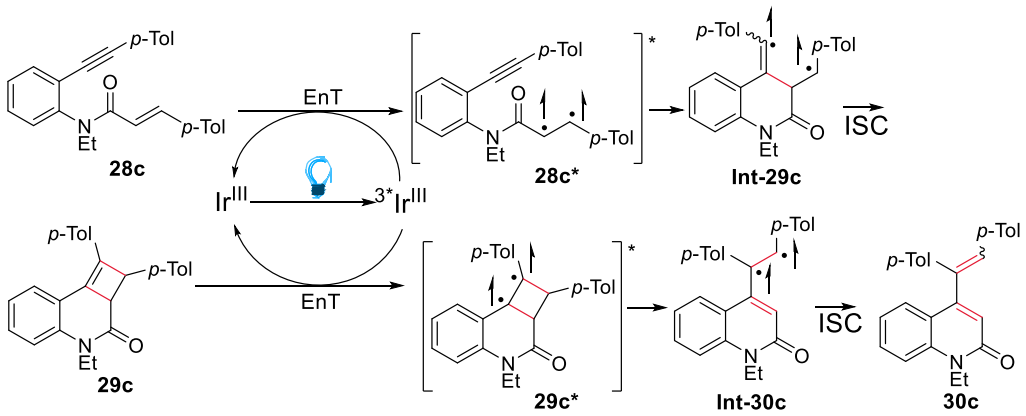


Figure 3-8. Reaction mechanism of enyne photometathesis

3.6. Conclusion

We developed enyne photometathesis based on tandem energy transfer photocatalysis under visible light. Conjugated dienes could be formed via intramolecular cycloadditions of conjugated enynes. Triplet tandem activation is responsible for the ring-opening from cyclobutene as an intermediate. In an aspect of synthetic chemistry, the photo-cycloaddition of enyne can offer alternative methods to the transition metal catalytic enyne metathesis resulting conjugated dienes with high substitution. This finding is meaningful because 1,3-diene product in the reaction can include bioactive molecules such as coumarin and 2-quinolone. Furthermore, We proved the applicability of our synthetic tool toward formation of a variety of extended π-system.

3.7. Experimental Procedure and Data

Stern-Volmer luminescence quenching experiments

Stern-Volmer luminescence quenching studies were carried out using a 0.1 mM solution of photocatalyst and variable concentrations of substrate in dry DCM under Ar gas at rt. Samples were prepared in 0.5 mL quartz cuvettes inside an argon filled glove-box, and sealed with parafilm. The solutions were irradiated at 420 nm and the luminescence was measured at maximum emission wavelength of each photocatalyst. (I_0 = emission intensity of the photocatalyst in isolation at the specified wavelength; I = observed intensity as a function of the quencher concentration)

Electrochemical measurements with cyclic voltammogram

Electrochemical measurement :

Samples for electrochemical measurements were prepared with 0.03 mmol of substrate in anhydrous degassed 0.1 M Bu_4NPF_6 solution in MeCN (3 mL). The corresponding cyclic voltammograms were collected by a Potentiostat equipped with a reference electrode (3 M KCl Ag/AgCl), counter electrode (platinum wire) and working electrode (glassy carbon), and 100 mV/s (scan rate); Data were analyzed by subtracting the electrolyte solution background current prior to identifying the maximum current (Cp) and determining the potential ($E_{p/2}$) at half this value ($C_{p/2}$). The obtained value was referenced to Ag/AgCl and converted to SCE by subtracting 0.04 V.

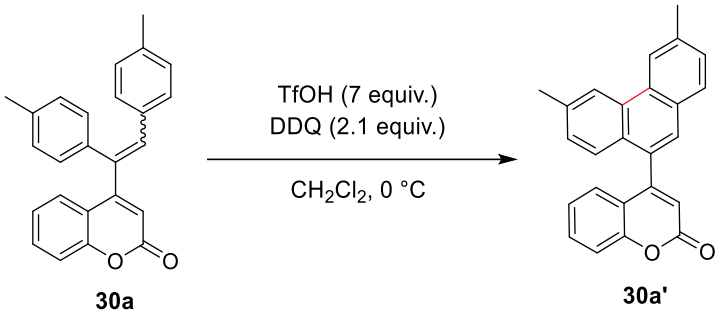
General Procedure B **(1,3-diene synthesis)**

In a dried 4 mL vial, catalyst $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5 mol%) and enyne (1.0 equiv., 0.1 mmol) were equipped. The heterogenic mixture was dissolved in CH_2Cl_2 (2 mL) under Ar gas in the glovebox. And then the solution was put under blue light from 12 W LED strip at ambient temperature maintaining by a cooling fan. The solution was put under nitrogen blow after finishing reaction with monitoring by TLC technique. Column flash chromatography separated the residue on silica gel to obtain desired product.

Synthesis of Extended π-Systems

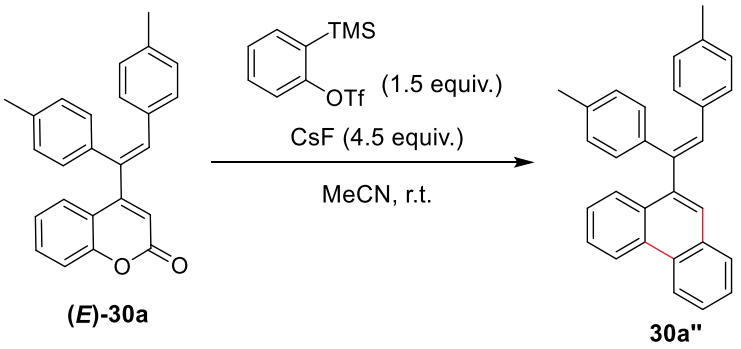
Step 1 : In a dried 4 mL vial, catalyst $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5 mol%) and enyne **28s**, **28t** or **28u** (1.0 equiv., 0.1 mmol) were equipped. The heterogenic mixture was dissolved in CH_2Cl_2 (2 mL) under Ar gas in the glovebox. And then the solution was put under blue light from 12 W LED strip at ambient temperature maintaining by a cooling fan. The solution was put under nitrogen blow after finishing reaction with monitoring by TLC technique. Column flash chromatography separated the residue on silica gel to obtain desired product **29s′, 29t′** or **29u′**.

Step 2 : Solution of **29t′** or **29u′** in *o*-xylene was stirred at 100 °C. The solution was put under nitrogen blow after finishing reaction with monitoring by TLC technique. Column flash chromatography separated the residue on silica gel the desired product **30t′**, **30u′**.



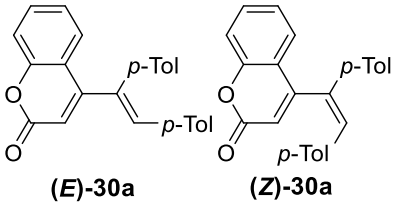
30a **30a'**

To a mixture of diene **30a** (0.2 mmol, 1.0 equiv.) and DDQ (2.1 equiv.) in dry CH_2Cl_2 (7 mL, 0.03 M) at 0°C was added trifluoromethanesulfonic acid (7.0 equiv.) dropwise. The reaction mixture was stirred at 0 °C for 3 hours. The mixture was quenched by saturated $NaHCO_3$ solution and extracted by CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. Column Flash chromatography separated the residue on silica gel to give the desired product **30a′**. 43 mg, 61% yield; white solid; m.p. 199 – 200 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.54 (s, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.64 (s, 1H), 7.55 – 7.42 (m, 4H), 7.32 (d, *J* = 8.3 Hz, 1H), 7.08 – 7.00 (m, 2H), 6.57 (s, 1H), 2.67 (s, 3H), 2.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 155.6, 153.7, 137.5, 136.9, 131.9, 130.6, 130.5, 130.2, 129.0, 128.9, 128.8, 128.7, 127.8, 127.6, 126.5, 126.2, 124.2, 122.9, 122.4, 120.1, 117.1, 116.7, 22.2, 22.0; HRMS *m/z* calculated for $[C_{25}H_{19}O_2]^+$ ($[M+H]^+$): 351.1380, observed 351.1380.



To a solution of diene **(*E*)-30a** (0.045 mmol, 1.0 equiv.) and 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (1.5 equiv.) in THF (0.45 mL, 0.1 M) was added cesium fluoride (4.5 equiv.). The reaction mixture was stirred at room temperature for 18 hours. The reaction mixture was concentrated under vacuum. Column Flash chromatography separated the residue on silica gel to obtained the desired product. 11 mg, 64% yield of **30a"**; White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (t, *J* = 8.4 Hz, 2H), 8.08 (d, *J* = 8.3 Hz, 1H), 7.89 (d, *J* = 7.7 Hz, 1H), 7.69 – 7.55 (m, 3H), 7.46 (ddq, *J* = 8.1, 6.9, 1.3 Hz, 1H), 7.21 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 7.7 Hz, 2H), 7.00 (d, *J* = 7.8 Hz, 2H), 6.83 (s, 1H), 2.34 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.9, 140.8, 137.5, 137.0, 136.7, 134.6, 131.6, 131.2, 130.8, 130.7, 130.1, 129.5, 129.4, 129.0, 128.8, 128.6, 127.9, 127.2, 126.7, 126.5, 126.4, 126.2, 122.8, 122.5, 76.7, 21.3; HRMS *m/z* calculated for $[C_{30}H_{24}Na]^+$ ($[M+Na]^+$): 407.1770, observed 407.1770.

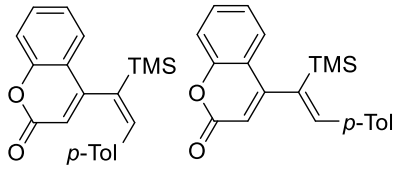
4-(1,2-di-*p*-tolylvinyl)-2*H*-chromen-2-one (30a)



Prepared according to the ***General Procedure B*** using 2-(*p*-tolylethynyl)phenyl *(E)*-3-(*p*-tolyl)acrylate **28a** (0.1 mmol, 1.0 equiv.), 26 mg, 73% yield, (*E/Z* 1:1); ***(E)*-30a**: pale yellow solid; m.p. 144 – 146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.45 (ddd, *J* = 8.7, 7.3, 1.6 Hz, 1H), 7.34 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.16 – 7.06 (m, 7H), 7.03 (d, *J* = 8.2 Hz, 2H), 6.83 (s, 1H), 6.41 (s, 1H), 2.33 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 157.8, 154.2, 138.3, 138.2, 136.2, 135.0, 133.0, 132.8, 131.6, 129.8, 129.8, 129.4, 129.1, 127.3, 124.1, 119.2, 117.3, 115.7, 21.45, 21.45; HRMS m/z calculated for $[C_{25}H_{21}O_2]$+ ($[M+H]^+$): 353.1536, observed : 353.1536; **(*Z*)-30a** : pale yellow solid;

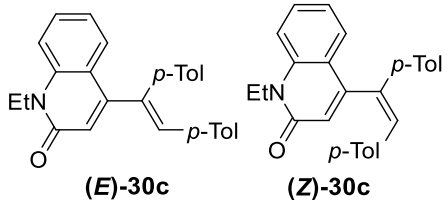
m.p. 76 – 77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (t, *J* = 7.8 Hz, 1H), 7.47 – 7.36 (m, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.23 (s, 1H), 7.15 (d, *J* = 8.4 Hz, 2H), 7.14 – 7.09 (m, 1H), 7.05 (d, *J* = 8.1 Hz, 2H), 6.98 (d, *J* = 8.2 Hz, 2H), 6.35 (s, 1H), 2.35 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 160.9, 155.5, 154.3, 138.4, 138.1, 137.2, 134.6, 133.0, 132.1, 130.9, 129.7, 129.4, 128.9, 127.1, 126.3, 124.7, 119.2, 117.4, 117.2, 21.32, 21.28; HRMS m/z calculated for $[C_{25}H_{21}O_2]^+$ ($[M+H]^+$): 353.1536, observed : 353.1536

4-(2-(*p*-tolyl)-1-(trimethylsilyl)vinyl)-2*H*-chromen-2-one (30b)



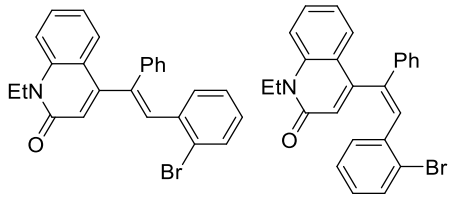
Prepared according to the ***General Procedure B*** using 2-((trimethylsilyl)ethynyl)phenyl *(E)*-3-(*p*-tolyl)acrylate **28b** (0.1 mmol, 1.0 equiv.), 20 mg, 60% yield (*E/Z* 1.2:1); white solid; m.p. 103 – 116 °C; The NMR spectrum was obtained on a partially purified material as a mixture of *E/Z* isomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, *J* = 7.9, 1.6 Hz, 0.4H), 7.54 (ddd, *J* = 8.6, 7.3, 1.6 Hz, 0.4H), 7.49 (ddd, *J* = 8.6, 7.2, 1.6 Hz, 0.6H), 7.43 (dd, *J* = 7.9, 1.6 Hz, 0.6H), 7.37 (m, 1H), 7.32 – 7.24 (m, 1.6H), 7.20 (d, *J* = 7.8 Hz, 0.8H), 7.13 (t, *J* = 7.6 Hz, 0.6H), 7.04 (d, *J* = 8.0 Hz, 1.2H), 7.00 (s, 0.6H), 6.94 (d, *J* = 8.0 Hz, 1.2H), 6.16 (s, 0.4H), 6.13 (s, 0.6H), 2.39 (s, 1.2H), 2.22 (s, 1.8H), 0.16 (s, 5.4H), 0.01 (s, 3.6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 161.1, 160.9, 158.9, 153.8, 153.7, 146.4, 140.1, 140.0, 138.4, 138.1, 138.0, 135.2, 133.3, 132.0, 131.8, 129.2, 128.9, 128.9, 128.4, 126.9, 126.7, 124.2, 124.0, 120.1, 118.2, 117.2, 117.2, 112.1, 111.8, 21.3, 21.1, 0.3, -1.5.; HRMS *m/z* calculated for $[C_{21}H_{23}O_2Si]^+$ ($[M+H]^+$): 335.1462, observed 335.1462.

4-(1,2-di-*p*-tolylvinyl)-1-ethylquinolin-2(1*H*)-one (30c)



Prepared according to the ***General Procedure B*** using *(E)*-*N*-ethyl-3-(*p*-tolyl)-*N*-(2-(*p*-tolylethynyl)phenyl)acrylamide **28c** (0.1 mmol, 1.0 equiv.), 30 mg, 80% yield, (*E/Z* 2:1); **(*E*)-30c :** yellow solid; m.p. 168 – 169 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.49 (ddd, *J* = 8.6, 7.1, 1.6 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.16 (d, *J* = 8.1 Hz, 2H), 7.10 – 6.99 (m, 7H), 6.74 (s, 1H), 6.73 (s, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 2.31 (s, 3H), 2.30 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 152.8, 139.3, 137.6, 137.5, 137.4, 135.8, 133.5, 131.5, 130.3, 129.4, 129.4, 129.2, 128.9, 128.0, 121.7, 121.6, 120.7, 114.2, 37.3, 21.25, 21.25, 12.8.; HRMS *m/z* calculated for $[C_{27}H_{25}NNaO]^+$ ($[M+Na]^+$): 402.1828, observed : 402.1820; **(*Z*)-30c :** white solid; m.p. 147 – 149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.39 (m, 3H), 7.33 – 7.23 (m, 3H), 7.18 (s, 1H), 7.10 (d, *J* = 7.6 Hz, 2H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.98 (d, *J* = 7.8 Hz, 2H), 6.90 (d, *J* = 7.7 Hz, 2H), 6.63 (s, 1H), 4.49 (dq, *J* = 14.1, 7.1 Hz, 1H), 4.36 (dq, *J* = 14.1, 7.1 Hz, 1H), 2.32 (s, 3H), 2.22 (s, 3H), 1.43 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 149.8, 139.3, 138.0, 137.8, 137.3, 136.0, 133.3, 130.6, 129.9, 129.3, 129.0, 128.8, 127.8, 126.1, 122.6, 122.1, 120.6, 114.3, 37.3, 21.12, 21.10, 12.9.; HRMS *m/z* calculated for $[C_{27}H_{25}NNaO]^+$ ($[M+Na]^+$): 402.1828, observed : 402.1820.

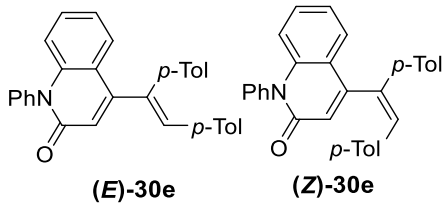
4-(2-(2-bromophenyl)-1-phenylvinyl)-1-ethylquinolin-2(1*H*)-one (30d)



(*E*)-30d **(*Z*)-30d**

Prepared according to the ***General Procedure B*** using *(E)*-3-(2-bromophenyl)-*N*-ethyl-*N*-(2-(phenylethynyl)phenyl)acrylamide **28d** (0.1 mmol, 1.0 equiv.). 32 mg, 74% yield (*E/Z* 1.8:1); yellow solid; The NMR spectrum was obtained on a partially purified material as a mixture of *E/Z* isomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 8.1, 1.3 Hz, 0.35H), 7.59 (t, *J* = 7.1 Hz, 1H), 7.54 – 7.48 (m, 1.35H), 7.46 – 7.30 (m, 3.35H), 7.20 – 7.13 (m, 3H), 7.11 – 7.00 (m, 3H), 7.01 – 6.92 (m, 0.65H), 6.93 – 6.87 (m, 0.35H), 6.87 (s, 0.65H), 6.83 (s, 0.65H), 6.63 (s, 0.35H), 4.50 – 4.25 (m, 2H), 1.40 (m, 1.45 –1.35, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 161.4, 151.7, 148.5, 140.1, 140.0, 139.3, 139.1, 139.0, 137.7, 137.2, 136.6, 132.59, 132.55, 131.4, 131.3, 130.6, 130.4, 130.3, 129.6, 129.3, 129.0, 128.9, 128.7, 128.5, 128.4, 127.99, 127.98, 127.8, 126.94, 126.93, 126.7, 124.7, 124.6, 123.2, 122.1, 122.0, 121.8, 120.7, 120.5, 114.4, 114.3, 37.4, 37.4, 12.9, 12.8; HRMS m/z calculated for $[C_{25}H_{21}BrNO]^+$ ($[M+H]^+$): 430.0801, observed 430.0799.

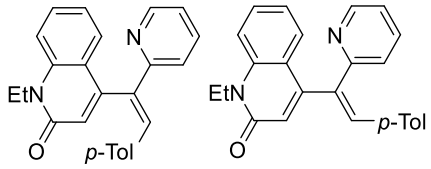
4-(1,2-di-*p*-tolylvinyl)-1-phenylquinolin-2(1*H*)-one (30e)



(*E*)-30e (*Z*)-30e

Prepared according to the ***General Procedure B*** using *(E)-N*-phenyl-3-(*p*-tolyl)-*N*-(2-(*p*-tolylethynyl)phenyl)acrylamide **28e** (0.1 mmol, 1.0 equiv.), 40 mg, 94% yield (*E/Z* 1.5:1); ***(E)*-30e** : white solid; m.p. 142 – 144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.0 Hz, 1H), 7.62 (m, 2H), 7.53 (m, 1H), 7.33 (d, *J* = 7.6 Hz, 2H), 7.29 – 7.21 (m, 3H), 7.10 (t, *J* = 7.4 Hz, 4H), 7.05 (t, *J* = 8.1 Hz, 3H), 6.83 (s, 2H), 6.67 (d, *J* = 8.5 Hz, 1H), 2.34 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 153.8, 141.4, 137.8, 137.7, 137.5, 137.5, 135.8, 133.4, 131.7, 130.2, 129.9, 129.5, 129.5, 129.3, 128.9, 128.9, 128.9, 127.4, 122.0, 122.0, 120.1, 116.3, 21.3, 21.3; HRMS *m/z* calculated for $[C_{31}H_{26}NO]^+$ ($[M+H]^+$): 428.2009, observed 428.2009; **(*Z*)-30e** : white solid; m.p. 144 – 146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.51 (m, 4H), 7.40 – 7.34 (m, 4H), 7.28 (ddd, *J* = 8.7, 7.1, 1.5 Hz, 1H), 7.24 (s, 1H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 8.1 Hz, 2H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.71 (m, 2H), 2.36 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1, 150.8, 141.4, 137.9, 137.9, 137.7, 137.5, 136.0, 133.3, 130.2, 130.2, 130.2, 130.1, 129.4, 129.1, 129.1, 129.0, 128.9, 128.8, 127.2, 126.2, 123.0, 122.5, 120.1, 116.3, 21.2, 21.1.; HRMS *m/z* calculated for $[C_{31}H_{26}NO]^+$ ($[M+H]^+$): 428.2009, observed 428.2009.

1-ethyl-4-(1-(pyridin-2-yl)-2-(*p*-tolyl)vinyl)quinolin-2(1*H*)-one (30f)

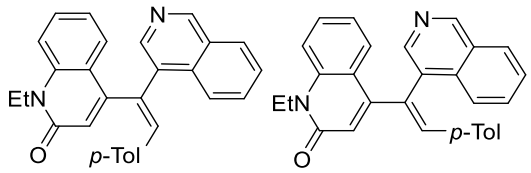


(*E*)-30f (*Z*)-30f

Prepared according to the ***General Procedure B*** using *(E)-N*-ethyl-*N*-(2-(pyridin-2-ylethynyl)phenyl)-3-(*p*-tolyl)acrylamide **28f** (0.1 mmol, 1.0 equiv.), 25 mg, 69% yield (*E/Z* 1:2.8); ***(E)*-30f :** yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (ddd, *J* = 4.8, 1.9, 0.9 Hz, 1H), 8.12 (s, 1H), 7.60 – 7.52 (m, 2H), 7.52 – 7.45 (m, 2H), 7.15 (ddd, *J* = 7.5, 4.8, 1.1 Hz, 1H), 7.11 – 7.02 (m, 3H), 6.97 (dt, *J* = 8.0, 1.0 Hz,

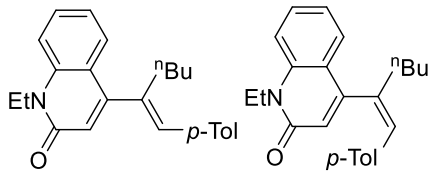
1H), 6.93 (d, *J* = 8.0 Hz, 2H), 6.70 (s, 1H), 4.53 (dq, *J* = 14.3, 7.2 Hz, 1H), 4.40 (dq, *J* = 14.0, 7.1 Hz, 1H), 2.24 (s, 3H) 1.46 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 156.6, 149.5, 149.0, 139.4, 138.2, 136.7, 133.9, 132.7, 130.9, 129.5, 129.1, 127.5, 123.0, 122.3, 121.4, 120.6, 114.4, 37.5, 21.2, 13.0; HRMS *m/z* calculated for $[C_{25}H_{23}N_2O]^+$ ($[M+H]^+$): 367.1805, observed : 367.1805; **(*Z*)-30f:** yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (ddd, *J* = 4.9, 1.7, 0.9 Hz, 1H), 7.81 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.56 (td, *J* = 7.7, 1.8 Hz, 1H), 7.50 (ddd, *J* = 8.6, 7.1, 1.5 Hz, 1H), 7.39 (d, *J* = 8.4 Hz, 1H), 7.29 (d, *J* = 7.9 Hz, 1H), 7.15 (ddd, *J* = 7.5, 4.9, 1.1 Hz, 1H), 7.10 – 7.05 (m, 1H), 7.04 – 6.97 (m, 4H), 6.96 (s, 1H), 6.75 (s, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 2.31 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 158.0, 151.6, 150.0, 139.3, 138.0, 137.3, 136.3, 134.6, 132.8, 130.3, 129.5, 128.9, 128.1, 125.0, 122.4, 122.0, 121.7, 120.7, 114.2, 37.3, 21.2, 12.7; HRMS *m/z* calculated for $[C_{25}H_{22}N_2NaO]^+$ ($[M+Na]^+$): 389.1624, observed : 389.1624.

1-ethyl-4-(1-(isoquinolin-4-yl)-2-(*p*-tolyl)vinyl)quinolin-2(1*H*)-one (30g)



Prepared according to the ***General Procedure B*** using *(E)-N*-ethyl-*N*-(2-(isoquinolin-1-ylethynyl)phenyl)-3-(*p*-tolyl)acrylamide **30g** (0.1 mmol, 1.0 equiv.), 34 mg, 82% yield (*E/Z* 1.5:1); yellow oil; The NMR spectrum was obtained on a partially purified material as a mixture of *E/Z* isomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.23 (s, 1H), 9.17 (s, 0.7H), 8.46 (s, 0.7H), 8.43 (s, 1H), 8.31 (d, *J* = 8.4 Hz, 0.7H), 8.19 (d, *J* = 8.1 Hz, 1.1H), 8.03 – 8.00 (m, 1.7H), 7.84 (d, *J* = 7.8 Hz, 1.1H), 7.78 (d, *J* = 8.0 Hz, 0.8H), 7.73 – 7.42 (m, 7.4H), 7.21 – 7.18 (m, 2.1H), 7.14 (s, 0.7H), 7.08 (d, *J* = 8.0 Hz, 1.4H), 7.02 (t, *J* = 7.5 Hz, 0.7H), 6.96 (d, *J* = 7.9 Hz, 1.4H), 6.88 – 6.82 (m, 4.1H), 6.71 (s, 0.7H), 6.57 (s, 1H), 4.53 – 4.28 (m, 4H), 2.26 (s, 2.1H), 2.21 (s, 3H), 1.41 – 1.35 (m, 5.2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 161.6, 152.7, 152.5, 152.0, 150.1, 144.2, 142.8, 139.8, 139.6, 138.4, 138.3, 137.5, 137.2, 134.1, 134.0, 133.7, 133.6, 132.9, 132.8, 131.3, 131.21, 131.17, 131.1, 130.9, 130.8, 129.4, 129.3, 129.2, 129.2, 129.0, 128.8, 128.51, 128.46, 127.6, 127.53, 127.52, 127.4, 124.6, 124.4, 122.9, 122.2, 122.1, 121.2, 120.5, 119.8, 114.8, 114.7, 37.6, 37.5, 21.4, 21.3, 13.0, 12.9; HRMS *m/z* calculated for $[C_{29}H_{25}N_2O]^+$ ($[M+H]^+$): 417.1961, observed : 417.1961.

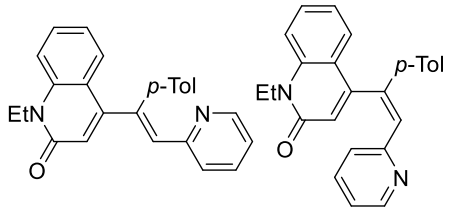
1-ethyl-4-(1-(*p*-tolyl)hex-1-en-2-yl)quinolin-2(1*H*)-one (30h)



(*E*)-30h **(*Z*)-30h**

Prepared according to the ***General Procedure B*** using *(E)-N*-ethyl-*N*-(2-(hex-1-yn-1-yl)phenyl)-3-(*p*-tolyl)acrylamide **28h** (0.1 mmol, 1.0 equiv.), 27 mg, 78% yield (*E/Z* 1.7:1); yellow oil; The NMR spectrum was obtained on a partially purified material as a mixture of *E/Z* isomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 8.0, 1.5 Hz, 0.7H), 7.65 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.59 – 7.52 (m, 1.9H), 7.44 – 7.41 (m, 1.9H), 7.28 – 7.26 (m, 0.6H), 7.22 – 7.19 (m, 1.9H), 7.13 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1.3H), 6.90 (d, *J* = 8.3 Hz, 2.2H), 6.86 (d, *J* = 8.2 Hz, 2.2H), 6.63 – 6.62 (m, 1.7H), 6.52 (s, 1H), 6.49 (s, 0.7H), 4.53 – 4.27 (m, 4.1H), 2.66 – 2.62 (m, 1.3H), 2.52 – 2.38 (m, 4.1H), 2.19 (s, 3H), 1.52 – 1.26 (m, 13H), 0.89 (t, *J* = 7.1 Hz, 3H), 0.82 (t, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 161.8, 153.3, 151.6, 139.4, 139.3, 139.0, 137.1, 136.9, 136.7, 134.0, 133.4, 130.8, 130.7, 130.6, 129.2, 129.0, 128.9, 128.8, 128.3, 127.6, 127.3, 122.1, 121.8, 121.0, 120.6, 120.1, 119.9, 114.5, 114.5, 40.0, 37.42, 37.39, 32.2, 30.7, 30.4, 22.9, 22.5, 21.4, 21.2, 14.0, 13.9, 13.0, 12.9; HRMS *m/z* calculated for $[C_{24}H_{28}NO]^+$ ($[M+H]^+$): 346.2165, observed : 346.2165.

1-ethyl-4-(2-(pyridin-2-yl)-1-(*p*-tolyl)vinyl)quinolin-2(1*H*)-one (30i)

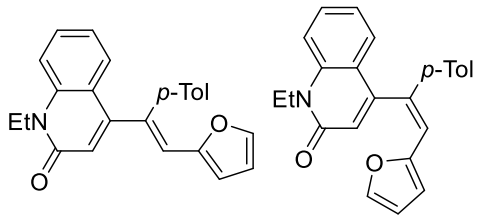


(*E*)-30i **(*Z*)-30i**

Prepared according to the ***General Procedure B*** using (*E*)-*N*-ethyl-3-(pyridin-2-yl)-*N*-(2-(*p*-tolylethynyl)phenyl)acrylamide **28i** (0.1 mmol, 1.0 equiv.), 27 mg, 74% yield (*E/Z* 1.3:1); **(*E*)-30i :** colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 – 8.59 (m, 1H), 7.71 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.49 (ddd, *J* = 8.6, 7.1, 1.5 Hz, 1H), 7.45 – 7.38 (m, 2H), 7.15 – 7.01 (m, 7H), 6.89 (s, 1H), 6.78 (s, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 2.30 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 156.0, 152.1, 149.7, 141.8, 139.4, 138.4, 135.7, 135.1, 131.8, 130.6, 129.6, 129.2, 128.1, 124.5, 122.0, 121.9, 121.8, 120.4, 114.4, 37.5, 21.4, 12.9; HRMS *m/z* calculated for $[C_{25}H_{23}N_2O]^+$ ($[M+H]^+$):

367.1805, observed : 367.1805; **(*Z*)-30i :** white solid; m.p. 131 – 133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 – 8.44 (m, 1H), 7.59 – 7.51 (m, 2H), 7.45 (d, *J* = 8.5 Hz, 1H), 7.40 – 7.30 (m, 4H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.08 – 7.04 (m, 1H), 6.99 – 6.94 (m, 2H), 6.64 (s, 1H), 4.50 (dq, *J* = 14.2, 7.1 Hz, 1H), 4.38 (dq, *J* = 14.1, 7.1 Hz, 1H), 2.33 (s, 3H), 1.44 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 155.1, 149.6, 149.5, 140.1, 139.4, 138.8, 137.1, 136.0, 130.9, 130.0, 129.6, 127.8, 126.6, 123.2, 122.3, 122.2, 121.8, 120.6, 114.5, 37.5, 21.3, 13.1; HRMS *m/z* calculated for $[C_{25}H_{23}N_2O]^+$ ($[M+H]^+$): 367.1805, observed : 367.1805

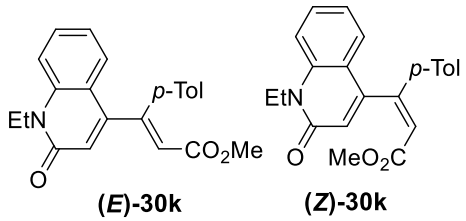
1-ethyl-4-(2-(furan-2-yl)-1-(*p*-tolyl)vinyl)quinolin-2(1*H*)-one (30j)



(*E*)-30j (*Z*)-30j

Prepared according to the ***General Procedure B*** using (*E*)-*N*-ethyl-3-(furan-2-yl)-*N*-(2-(*p*-tolylethynyl)phenyl)acrylamide **28j** (0.1 mmol, 1.0 equiv.), 36 mg, >99% yield (*E/Z* 1.2:1); brown viscous oil; **(*E*)-30j :** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.70 (m, 1H), 7.54 – 7.48 (m, 1H), 7.40 – 7.38 (m, 1H), 7.32 – 7.28 (m, 3H), 7.15 – 7.08 (m, 3H), 6.71 (s, 1H), 6.62 (s, 1H), 6.32 – 6.31 (m, 1H), 6.11 – 6.10 (m, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 2.35 (s, 3H), 1.38 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 152.4, 151.8, 142.3, 139.4, 138.1, 136.02, 135.96, 130.5, 129.4, 129.0, 128.1, 121.84, 121.75, 120.7, 120.2, 114.4, 111.6, 110.9, 37.5, 21.5, 12.9; HRMS *m/z* calculated for $[C_{24}H_{22}NO_2]^+$ ($[M+H]^+$): 356.1645, observed : 356.1645; **(*Z*)-30j :** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.45 (m, 3H), 7.31 – 7.29 (m, 2H), 7.19 – 7.03 (m, 5H), 6.70 (s, 1H), 6.20 – 6.19 (m, 1H), 5.87 (m, 1H), 4.57 – 4.35 (m, 2H), 2.32 (s, 3H), 1.46 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 151.9, 149.7, 142.5, 139.5, 138.2, 136.6, 133.9, 130.8, 129.6, 127.4, 126.0, 122.3, 122.3, 120.4, 117.0, 114.5, 111.8, 110.6, 37.6, 21.3, 13.1; HRMS *m/z* calculated for $[C_{24}H_{22}NO_2]^+$ ($[M+H]^+$): 356.1645, observed : 356.1645.

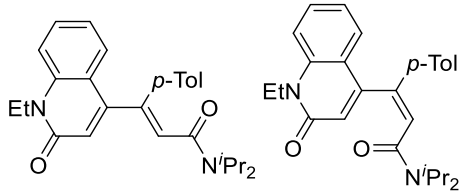
Methyl 3-(1-ethyl-2-oxo-1,2-dihydroquinolin-4-yl)-3-(*p*-tolyl)acrylate (30k)



(*E*)-30k (*Z*)-30k

Prepared according to the ***General Procedure B*** using methyl (*Z*)-4-(ethyl(2-(*p*-tolylethynyl)phenyl)amino)-4-oxobut-2-enoate **28k** (0.1 mmol, 1.0 equiv.), 21 mg, 60% yield, (*E/Z* 1.5:1); colorless oil; **(*E*)-30k:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 8.6 Hz, 1H), 7.27 (d, *J* = 8.7 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.08 (d, *J* = 7.8 Hz, 2H), 6.69 (s, 1H), 6.13 (s, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.71 (s, 3H), 2.23 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 161.2, 151.9, 150.4, 139.4, 139.2, 133.6, 130.7, 128.9, 128.6, 127.6, 121.9, 121.4, 120.6, 119.7, 114.4, 51.6, 37.4, 21.3, 12.7; HRMS *m/z* calculated for $[C_{22}H_{22}NO_3]^+$ ($[M+H]^+$): 348.1594, observed : 348.1590 **(*Z*)-30k:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (ddd, *J* = 8.6, 7.1, 1.5 Hz, 1H), 7.43 (d, *J* = 8.9 Hz, 1H), 7.39 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.34 (d, *J* = 8.3 Hz, 2H), 7.13 (d, *J* = 8.6 Hz, 2H), 7.07 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H), 6.62 (s, 1H), 6.55 (s, 1H), 4.52 – 4.34 (m, 2H), 2.34 (s, 3H), 1.39 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 161.4, 151.6, 148.6, 140.7, 138.9, 134.4, 130.5, 129.6, 127.1, 126.9, 122.0, 120.4, 120.3, 117.8, 114.4, 51.5, 37.5, 21.3, 12.9; HRMS *m/z* calculated for $[C_{22}H_{22}NO_3]^+$ ($[M+H]^+$): 348.1594, observed : 348.1594.

3-(1-ethyl-2-oxo-1,2-dihydroquinolin-4-yl)-*N,N*-diisopropyl-3-(*p*-tolyl)acrylamide (30l)

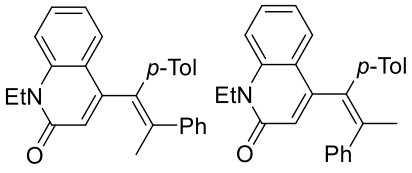


(*E*)-30l (*Z*)-30l

Prepared according to the ***General Procedure B*** using N^1-ethyl-N^4,N^4-diisopropyl-N^1-(2-(*p*-tolylethynyl)phenyl)maleamide **28l** (0.1 mmol, 1.0 equiv.), 34 mg, 82% yield (*E/Z* 1:2.4); yellow oil; The NMR spectrum was obtained on a partially purified material as a mixture of *E/Z* isomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.27 (m, 7.52H), 7.14 – 7.01 (m, 4.92H), 6.77 (s, 1H), 6.76 (s, 0.5H), 6.59 (s, 0.5H), 6.21 (s, 1H), 4.43 – 4.35 (m, 3H), 4.21 – 4.14 (m, 1.5H), 3.46 – 3.32 (m, 1.5H), 2.33 (s, 1.5H), 2.30 (s, 3H), 1.47 – 1.36 (m, 11H), 1.26 – 1.20 (m, 5.3H), 1.13 – 1.10 (m, 1.3H), 0.85 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 165.9, 161.7, 161.4, 150.8, 148.6, 142.9, 140.1, 139.2, 139.1,

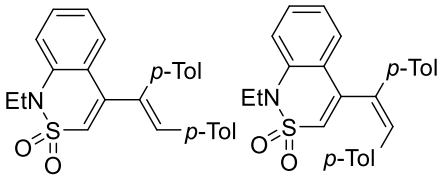
139.1, 138.9, 135.7, 134.3, 130.7, 130.5, 129.7, 129.3, 128.4, 128.4, 128.3, 127.7, 126.5, 126.5, 125.5, 122.0, 122.0, 121.5, 121.4, 120.7, 120.2, 114.3, 53.5, 50.6, 45.9, 45.6, 37.5, 37.4, 30.2, 29.8, 21.4, 21.3, 20.6, 20.3, 13.0, 12.9; HRMS *m/z* calculated for $[C_{27}H_{33}N_2O_2]^+$ ($[M+H]^+$): 417.2537, observed : 417.2532.

1-ethyl-4-(2-phenyl-1-(*p*-tolyl)prop-1-en-1-yl)quinolin-2(1*H*)-one (30m)



Prepared according to the ***General Procedure B*** using (*E*)-*N*-ethyl-3-(*p*-tolyl)-*N*-(2-(*p*-tolylethynyl)phenyl)but-2-enamide **28m** (0.1 mmol, 1.0 equiv.), 16 mg, 43% yield (*E/Z* = 1.2:1); yellow solid; m.p. 86 – 88 °C; The NMR spectrum was obtained on a partially purified material as a mixture of *E/Z* isomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.9 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 0.6H), 7.46 – 7.37 (m, 1H), 7.34 – 7.02 (m, 8H), 6.92 (d, *J* = 8.0 Hz, 1.2H), 6.84 (d, *J* = 8.0 Hz, 1.2H), 6.75 (s, 0.6H), 6.49 (s, 0.4H), 4.50 – 4.29 (m, 1.6H), 4.14 (dq, *J* = 14.1, 7.1 Hz, 0.4H), 2.32 (s, 1.2H), 2.27 (s, 1.2H), 2.17 (s, 1.8H), 2.02 (s, 1.8H), 1.41 (t, *J* = 7.1 Hz, 1.8H), 1.26 (t, *J* = 7.1 Hz, 1.2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 161.6, 152.0, 151.8, 143.1, 142.6, 139.4, 139.1, 138.9, 137.8, 137.4, 137.00, 136.97, 136.2, 134.4, 133.7, 130.5, 130.0, 129.6, 129.1, 129.05, 129.01, 128.6, 128.1, 128.08, 128.04, 127.6, 127.4, 126.8, 126.8, 122.9, 122.0, 121.6, 121.5, 121.2, 120.5, 114.4, 114.1, 37.4, 37.0, 23.4, 22.8, 21.2, 21.0, 12.9, 12.8; HRMS m/z calculated for $[C_{27}H_{26}NO]^+$ ($[M+H]^+$): 380.2009, observed

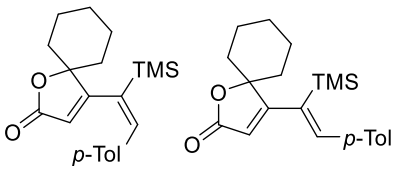
4-(1,2-di-*p*-tolylvinyl)-1-ethyl-1H-benzo[*c*][1,2]thiazine 2,2-dioxide (30n)



Prepared according to the ***General Procedure B*** using (*E*)-*N*-ethyl-2-(*p*-tolyl)-*N*-(2-(*p*-tolylethynyl)phenyl)ethene-1-sulfonamide **28n** (0.1 mmol, 1.0 equiv.), 25 mg, 60% yield (*E/Z* 1.3:1); **(*E*)-30n:** white solid; m.p.110 –111 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.38 (td, *J* = 7.8, 7.1, 1.5 Hz, 1H), 7.28 – 7.26 (m, 1H), 7.08 – 6.99 (m, 9H), 6.85 (s, 1H), 6.78 (s, 1H),

4.09 (q, *J* = 7.1 Hz, 2H), 2.31 (s, 3H), 2.29 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.5, 139.6, 138.1, 138.0, 137.2, 135.1, 133.6, 133.2, 130.9, 129.9, 129.8, 129.6, 129.5, 129.1, 122.98, 122.96, 122.6, 118.6, 41.8, 21.4, 21.4, 14.7; HRMS *m/z* calculated for $[C_{26}H_{25}NNaO_2S]^+$ ($[M+Na]^+$): 438.1498, observed : 438.1498; **(*Z*)-30n:** colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.41 (m, 2H), 7.32 (d, *J* = 8.3 Hz, 1H), 7.28 – 7.26 (m, 2H), 7.19 (s, 1H), 7.14 – 7.10 (m, 4H), 7.03 – 6.98 (m, 3H), 6.66 (s, 1H), 4.27 – 4.12 (m, 2H), 2.32 (s, 3H), 2.27 (s, 3H), 1.45 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 139.8, 138.2, 138.1, 137.3, 135.2, 132.7, 131.3, 131.0, 129.6, 129.4, 129.3, 129.1, 126.1, 123.2, 122.7, 122.4, 117.9, 40.9, 21.4, 21.3, 14.9; HRMS *m/z* calculated for $[C_{26}H_{25}NNaO_2S]^+$ ($[M+Na]^+$): 438.1498, observed : 438.1499.

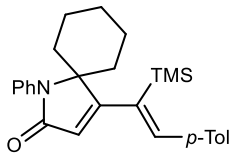
4-(2-(*p*-tolyl)-1-(trimethylsilyl)vinyl)-1-oxaspiro[4.5]dec-3-en-2-one (30o)



(*E*)-30o **(*Z*)-30o**

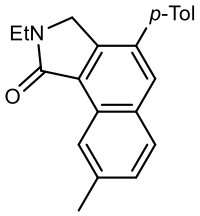
Prepared according to the ***General Procedure B*** using 1-((trimethylsilyl)ethynyl)cyclohexyl (*E*)-3-(*p*-tolyl)acrylate **28o** (0.05 mmol, 1.0 equiv.) and CH_2Cl_2 (5 mL, 0.01 M), 24 mg, 70% yield (*E/Z* 1:1); **(*E*)-30o:** white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.1 Hz, 2H), 7.06 (d, *J* = 8.0 Hz, 2H), 6.90 (s, 1H), 5.85 (s, 1H), 2.32 (s, 3H), 1.65 – 1.47 (m, 6H), 1.37 – 1.23 (m, 4H), 0.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.6, 172.1, 141.4, 138.6, 136.6, 135.6, 129.2, 129.1, 117.0, 91.7, 34.6, 24.5, 22.3, 21.5, 0.2; HRMS *m/z* calculated for $[C_{21}H_{28}NaO_2Si]^+$ ($[M+Na]^+$): 363.1751, observed : 363.1762; **(*Z*)-30o:** white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 – 7.16 (m, 5H), 5.62 (s, 1H), 2.37 (s, 3H), 1.81 – 1.60 (m, 10H), 0.02 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.6, 175.3, 146.1, 138.3, 137.4, 135.5, 129.0, 128.6, 114.9, 90.1, 34.0, 24.8, 22.3, 21.4, 1.5; HRMS *m/z* calculated for $[C_{21}H_{29}O_2Si]^+$ ($[M+H]^+$): 341.1931, observed : 341.1931

(*Z*)-1-phenyl-4-(2-(*p*-tolyl)-1-(trimethylsilyl)vinyl)-1-azaspiro[4.5]dec-3-en-2-one (30p)



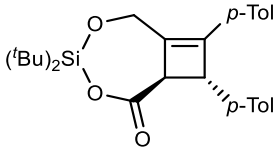
Prepared according to the ***General Procedure B*** using (*E*)-*N*-phenyl-3-(*p*-tolyl)-*N*-(1-((trimethylsilyl)ethynyl)cyclohexyl)acrylamide **28p** (0.1 mmol, 1.0 equiv.), 25 mg, 60% yield; white solid; m.p. 174 – 176 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.37 (m, 3H), 7.26 – 7.23 (m, 3H), 7.21 – 7.16 (m, 4H), 5.82 (s, 1H), 2.38 (s, 3H), 2.02 – 1.96 (m, 2H), 1.89 – 1.82 (m, 2H), 1.72 – 1.63 (m, 2H), 1.45 – 1.27 (m, 4H), 0.06 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 171.0, 147.1, 140.1, 138.0, 137.8, 136.0, 131.5, 129.3, 128.9, 128.5, 128.5, 120.7, 70.3, 33.8, 25.0, 22.4, 21.4, 1.7; HRMS *m/z* calculated for $[C_{27}H_{34}NOSi]^+$ ($[M+H]^+$): 416.2404, observed : 416.2404

2-ethyl-8-methyl-4-(*p*-tolyl)-2,3-dihydro-1H-benzo[*e*]isoindol-1-one (30q′)



Prepared according to the ***General Procedure B*** using (*E*)-*N*-ethyl-3-(*p*-tolyl)-*N*-(3-(*p*-tolyl)prop-2-yn-1-yl)acrylamide **28q** (0.1 mmol, 1.0 equiv.), 17 mg, 54% yield; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.49 (s, 1H), 7.37 – 7.35 (m, 3H), 7.28 (d, *J* = 8.0 Hz, 2H), 4.27 (s, 2H), 3.67 (q, *J* = 7.3 Hz, 2H), 2.49 (s, 3H), 2.43 (s, 3H), 1.24 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 137.8, 137.6, 135.0, 134.2, 134.1, 133.7, 131.8, 129.8, 129.7, 129.64, 129.63, 128.4, 124.9, 123.0, 49.2, 37.3, 22.2, 21.5, 13.6; HRMS *m/z* calculated for $[C_{22}H_{22}NO]^+$ ($[M+H]^+$): 316.1696, observed : 316.1697

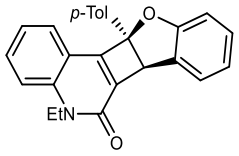
4,4-di-*tert*-butyl-8,9-di-*p*-tolyl-3,5-dioxa-4-silabicyclo[5.2.0]no*N*-7-en-2-one (29r)



Prepared according to the ***General Procedure B*** using di-*tert*-butyl((3-(*p*-tolyl)prop-2-yn-1-yl)oxy)silyl (*E*)-3-(*p*-tolyl)acrylate **28r** (0.1 mmol, 1.0 equiv.), 28 mg, 62% yield; white solid; m.p. 68 – 70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.0 Hz, 2H), 7.14 – 7.05 (m, 4H), 7.02 (d, *J* = 8.1 Hz, 2H), 5.22 (dt, *J* = 15.8, 1.8 Hz, 1H), 4.95 (dt, *J* = 15.9, 2.3 Hz, 1H), 4.45 (d, *J* = 2.1 Hz, 1H), 3.61 (d, *J* = 1.7 Hz, 2H), 2.32 (s, 3H), 2.31 (s, 3H), 1.07 (s, 9H), 1.06 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 69.0, 142.2,

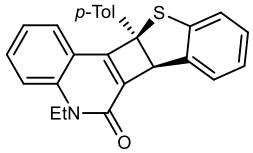
138.2, 137.0, 136.5, 133.9, 130.1, 129.3, 129.3, 127.1, 127.0, 62.5, 56.1, 48.7, 27.3, 27.0, 21.3, 21.1, 21.0.. HRMS *m/z* calculated for $[C_{28}H_{37}O_3Si]^+$ ($[M+H]^+$): 449.2506, observed 449.2506.

12-ethyl-5-(*p*-tolyl)-5a,12-dihydro-11*H*-benzofuro[2',3':1,4]cyclobuta[1,2-*c*]quinolin-11-one (29s′)



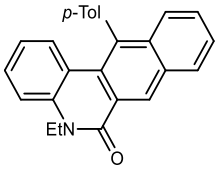
28 mg, 74% yield; white solid; m.p. 152 – 153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.49 (m, 3H), 7.43 (dd, *J* = 7.9, 5.7 Hz, 3H), 7.23 – 7.13 (m, 4H), 6.94 (t, *J* = 7.2 Hz, 2H), 4.89 (s, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 2.37 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 157.5, 151.2, 142.0, 138.7, 137.3, 134.8, 130.6, 129.5, 129.1, 126.9, 126.1, 125.7, 125.3, 122.3, 121.6, 117.2, 115.6, 111.3, 93.4, 60.0, 37.7, 21.4, 13.2; HRMS *m/z* calculated for $[C_{26}H_{22}NO_2]^+$ ($[M+H]^+$): 380.1645, observed : 380.1645.

5-ethyl-11a-(*p*-tolyl)-6b,11a-dihydrobenzo[4',5']thieno[2',3':3,4]cyclobuta[1,2-c]quinolin-6(5*H*)-one (29t′)



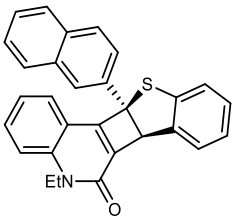
40 mg, >99% yield; white solid; m.p. 146 – 147 °C ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.61 – 7.55 (m, 2H), 7.46 (d, *J* = 8.2 Hz, 3H), 7.27 – 7.18 (m, 2H), 7.18 – 7.12 (m, 4H), 5.09 (s, 1H), 4.35 (qd, *J* = 7.0, 2.6 Hz, 2H), 2.35 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0, 152.8, 142.1, 141.9, 138.0, 136.6, 134.2, 131.7, 130.4, 129.4, 128.4, 127.2, 126.1, 125.2, 125.0, 122.6, 122.1, 116.9, 115.7, 68.6, 66.9, 37.5, 21.1, 13.1.; HRMS *m/z* calculated for $[C_{26}H_{22}NOS]^+$ ($[M+H]^+$): 396.1417, observed 396.1421.

5-ethyl-12-(*p*-tolyl)benzo[*j*]phenanthridin-6(5*H*)-one (30t′)



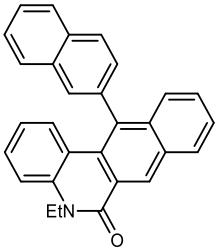
65% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.28 (s, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 8.7 Hz, 1H), 7.54 (ddd, *J* = 8.1, 6.7, 1.3 Hz, 1H), 7.47 (ddd, *J* = 8.3, 6.7, 1.3 Hz, 1H), 7.41 (d, *J* = 7.9 Hz, 2H), 7.39 – 7.30 (m, 3H), 7.25 (d, *J* = 9.1 Hz, 2H), 6.78 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1H), 4.48 (q, *J* = 7.1 Hz, 2H), 2.55 (s, 3H), 1.47 (t, *J* = 7.1 Hz, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 137.8, 137.5, 137.3, 136.5, 135.7, 131.8, 130.31, 130.26, 130.1, 129.4, 129.3, 128.4, 128.0, 127.6, 126.9, 126.2, 124.5, 121.1, 120.9, 114.7, 38.2, 21.5, 12.7.; HRMS *m/z* calculated for $[C_{26}H_{22}NO]^+$ ($[M+H]^+$): 364.1696, observed 364.1697.

5-ethyl-11a-(naphthalen-2-yl)-6b,11a-dihydrobenzo[4',5']thieno[2',3':3,4]cyclobuta[1,2-c]quinolin-6(5*H*)-one (29u′)



33 mg, 76% yield; white solid; m.p. 205 – 206 °C ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (m, 1H), 7.87 – 7.83 (m, 2H), 7.76 – 7.70 (m, 3H), 7.63 – 7.59 (m, 2H), 7.51 – 7.44 (m, 3H), 7.29 – 7.16 (m, 4H) 5.21 (s, 1H), 4.41 – 4.35 (m, 2H), 1.37 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 152.9, 142.3, 142.2, 137.0, 134.3, 133.09, 133.05, 131.9, 130.7, 129.0, 128.7, 128.3, 127.8, 126.68, 126.67, 126.4, 126.0, 125.47, 125.45, 125.2, 122.8, 122.4, 117.1, 115.9, 68.6, 67.4, 37.7, 13.2; HRMS *m/z* calculated for $[C_{29}H_{22}NOS]^+$ ($[M+H]^+$): 432.1417, observed 432.1417.

5-ethyl-12-(naphthalen-2-yl)benzo[*j*]phenanthridin-6(5*H*)-one (30u′)



86% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (m, 1H), 8.15 (d, *J* = 8.2 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.87 – 7.85 (m, 2H), 7.64 – 7.50 (m, 5H), 7.45 – 7.41 (m, 1H), 7.39 – 7.34 (m, 2H), 7.31 – 7.27 (m, 1H), 6.61 (ddd, *J* = 8.4, 7.0, 1.3 Hz, 1H), 4.50 (q, *J* = 7.1 Hz, 2H), 1.49 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 138.6, 137.5, 136.3, 135.8, 134.1, 132.9, 132.0, 130.6, 129.61, 129.55, 129.5, 129.3, 128.9, 128.7, 128.4, 128.3, 128.2, 128.0, 127.0, 126.7, 126.6, 126.5, 124.7, 121.4, 120.8, 114.9, 38.4, 12.8; HRMS *m/z* calculated for $[C_{29}H_{22}NO]^+$ ($[M+H]^+$): 400.1696, observed 400.1696.

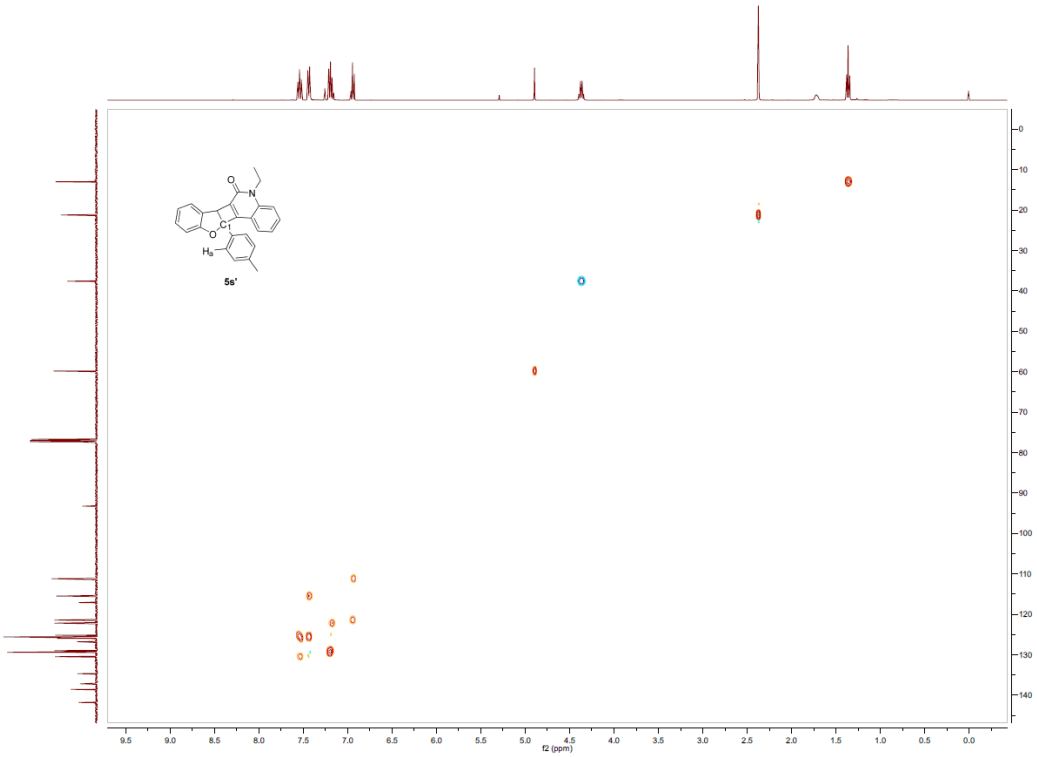


Figure 3-9. HSQC of compound 29s'

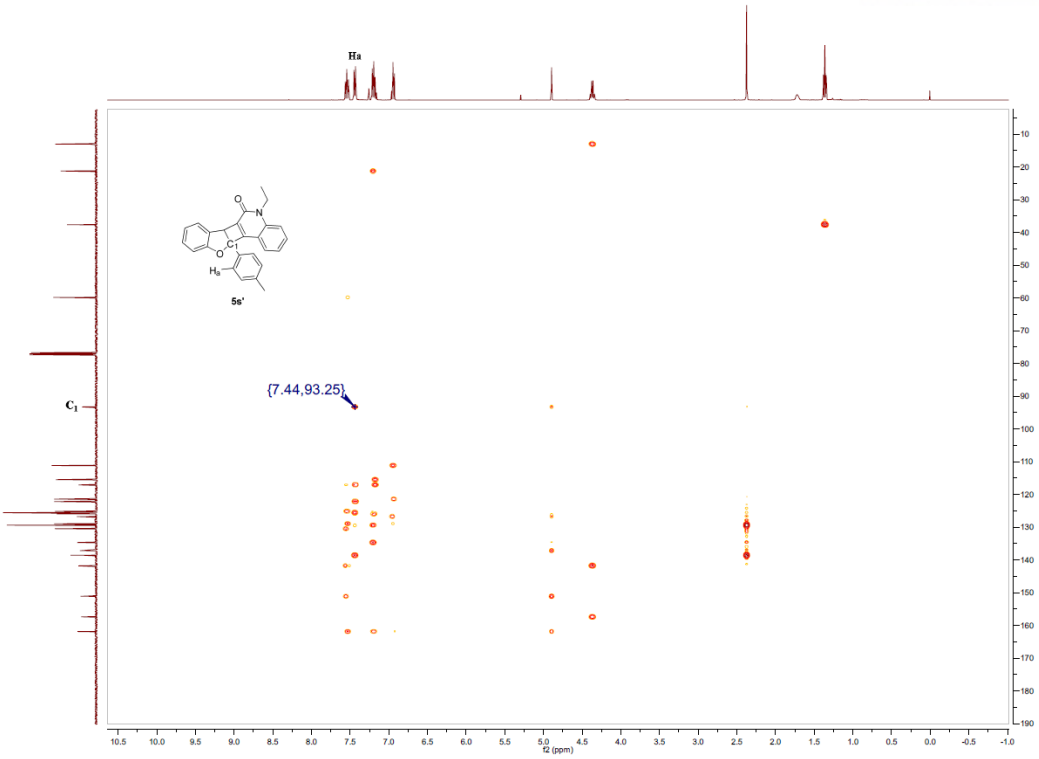


Figure 3-10. HMBC of compound 29s'

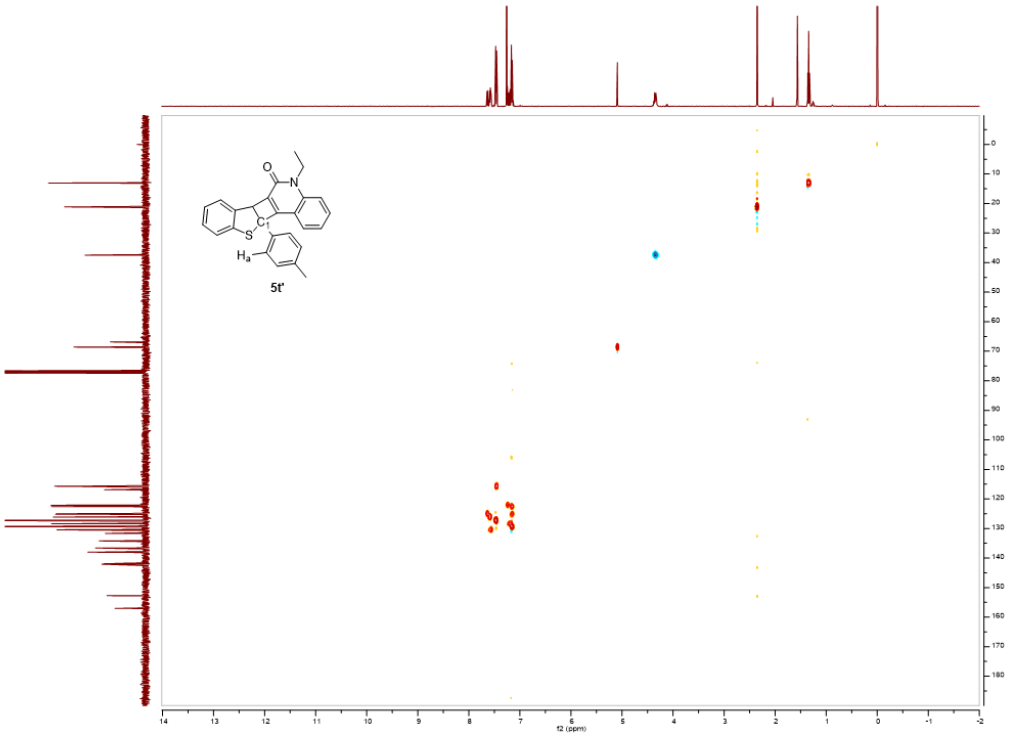


Figure 3-11. HSQC of compound 29t'

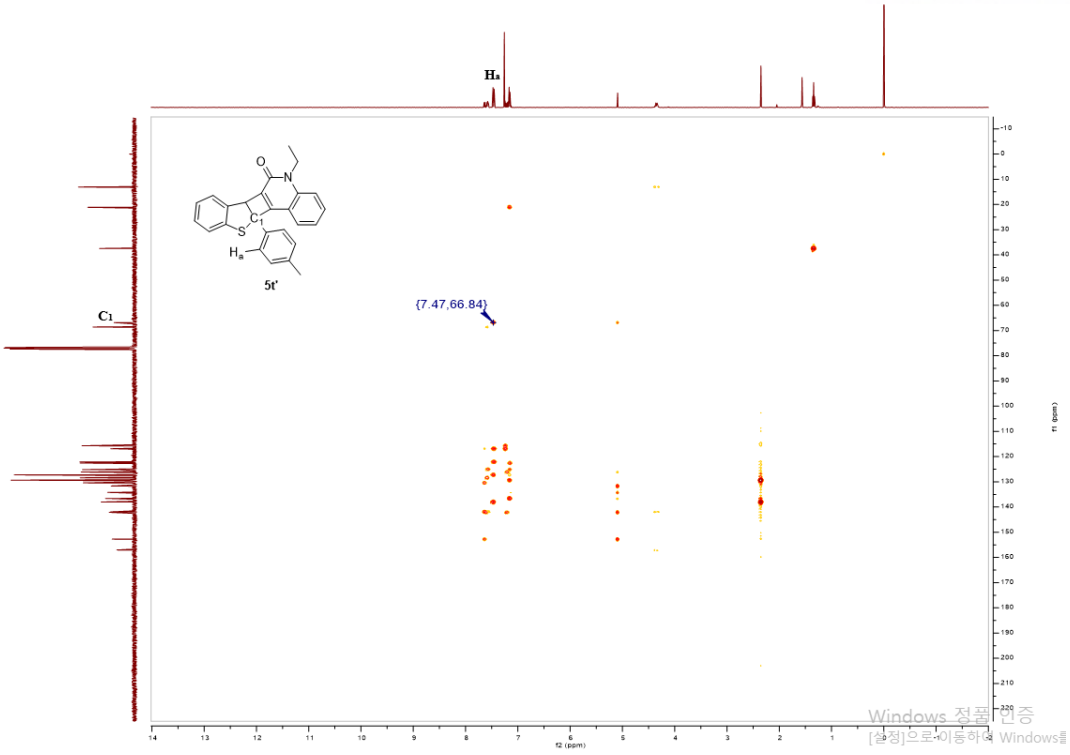


Figure 3-12. HMBC of compound 29t'

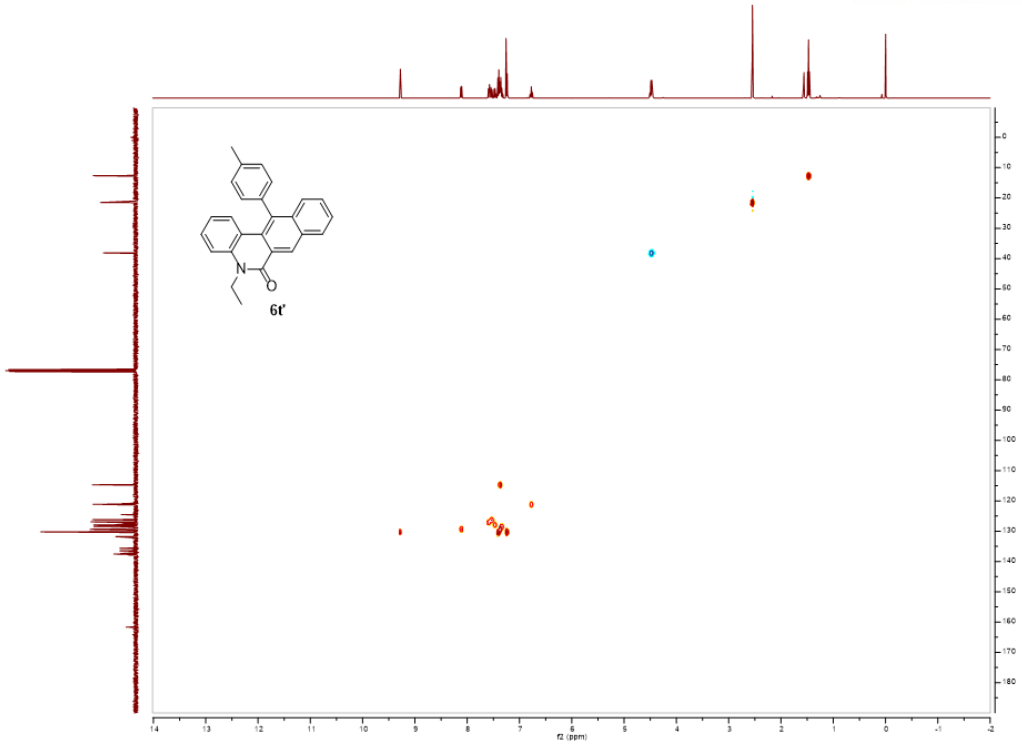


Figure 3-13. HSQC of compound 30t'

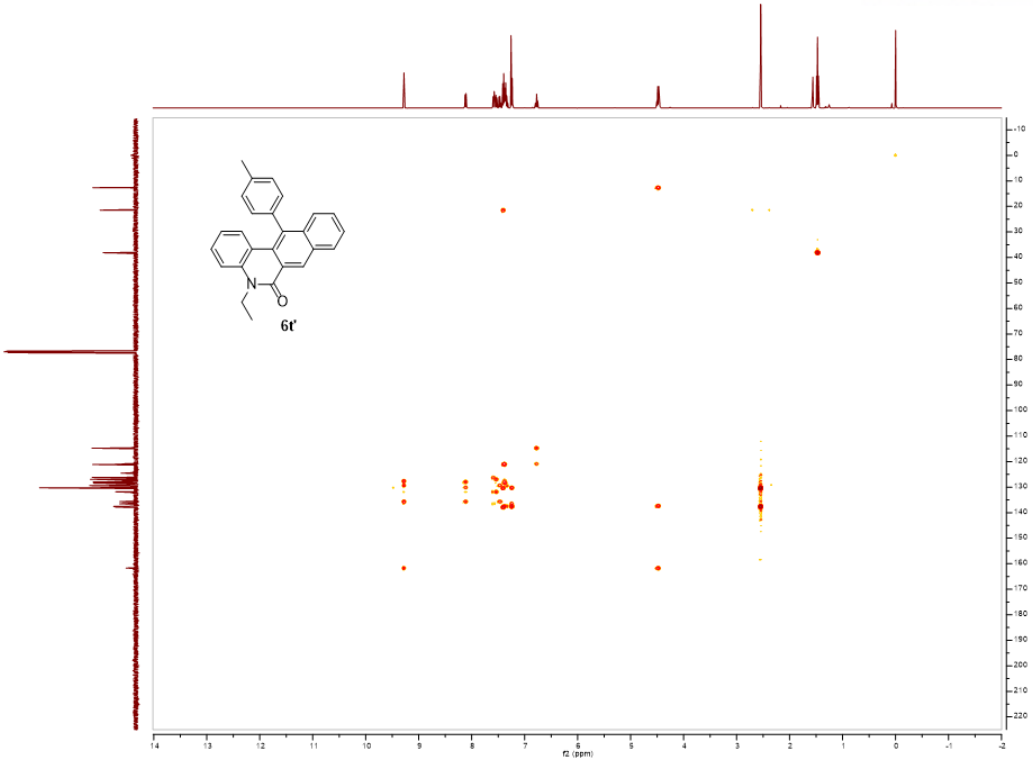


Figure 3-14. HMBC of compound 30t'

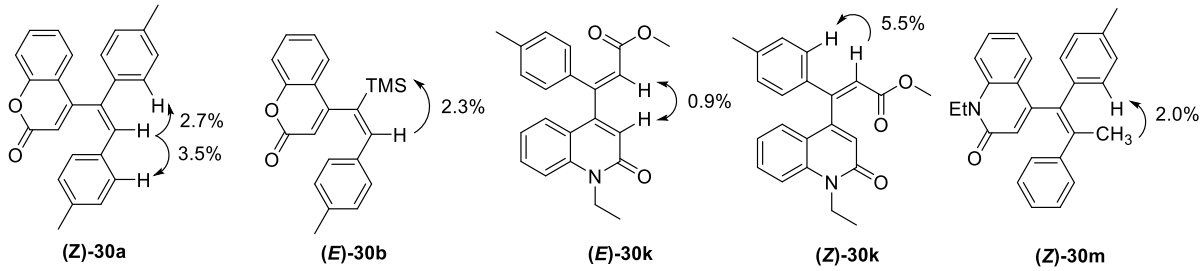


Figure 3-15. Stereochemical assignments by 1D NOE experiments

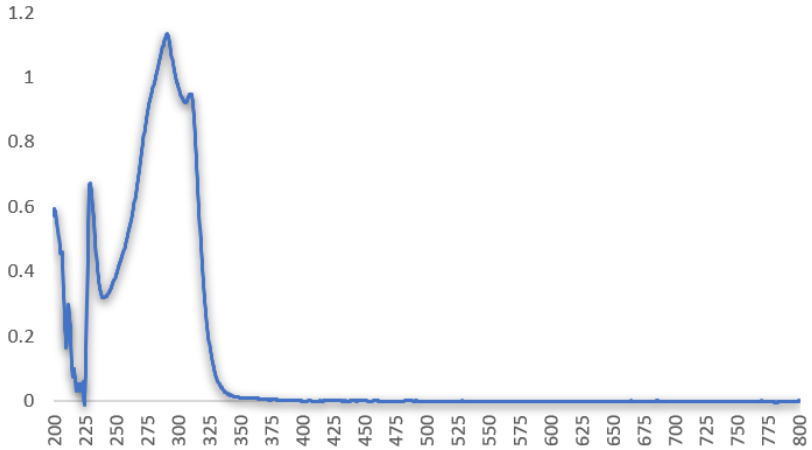


Figure 3-16. UV-Vis absorption spectrum data of 28c

References

1. Misale, A.; Niyomchon, S.; Maulide, N., Cyclobutenes: At a Crossroad between Diastereoselective Syntheses of Dienes and Unique Palladium-Catalyzed Asymmetric Allylic Substitutions. *Accounts of Chemical Research* **2016,** *49* (11), 2444-2458.
2. Xu, Y.; Conner, M. L.; Brown, M. K., Cyclobutane and cyclobutene synthesis: catalytic enantioselective [2+2] cycloadditions. *Angew Chem Int Ed Engl* **2015,** *54* (41), 11918-28.
3. Yujiro, H.; Koichi, N., Asymmetric [2+2] Cycloaddition Reaction Catalyzed by a Chiral Titanium Reagent. *Chemistry Letters* **1989,** *18* (5), 793-796.
4. Ito, H.; Hasegawa, M.; Takenaka, Y.; Kobayashi, T.; Iguchi, K., Enantioselective Total Synthesis of (+)-Tricycloclavulone. *Journal of the American Chemical Society* **2004,** *126* (14), 4520-4521.
5. Takenaka, Y.; Ito, H.; Iguchi, K., Enantioselective formal synthesis of (+)-precapnelladiene by chiral copper-catalyzed asymmetric [2+2]-cycloaddition reaction. *Tetrahedron* **2007,** *63* (2), 510-513.
6. Ishihara, K.; Fushimi, M., Catalytic Enantioselective [2 + 4] and [2 + 2] Cycloaddition Reactions with Propiolamides. *Journal of the American Chemical Society* **2008,** *130* (24), 7532-7533.
7. Schotes, C.; Mezzetti, A., Enantioselective Ficini Reaction: Ruthenium/PNNP-Catalyzed [2+2] Cycloaddition of Ynamides with Cyclic Enones. *Angewandte Chemie International Edition* **2011,** *50* (13), 3072-3074.
8. Enomoto, K.; Oyama, H.; Nakada, M., Highly Enantioselective Catalytic Asymmetric [2+2] Cycloadditions of Cyclic α-Alkylidene β-Oxo Imides with Ynamides. *Chemistry – A European Journal* **2015,** *21* (7), 2798-2802.
9. Shen, L.; Zhao, K.; Doitomi, K.; Ganguly, R.; Li, Y.-X.; Shen, Z.-L.; Hirao, H.; Loh, T.-P., Lewis Acid-Catalyzed Selective [2 + 2]-Cycloaddition and Dearomatizing Cascade Reaction of Aryl Alkynes with Acrylates. *Journal of the American Chemical Society* **2017,** *139* (38), 13570-13578.
10. Shibata, T.; Takami, K.; Kawachi, A., Rh-Catalyzed Enantioselective [2 + 2] Cycloaddition of Alkynyl Esters and Norbornene Derivatives. *Organic Letters* **2006,** *8* (7), 1343-1345.
11. Fan, B.-M.; Li, X.-J.; Peng, F.-Z.; Zhang, H.-B.; Chan, A. S. C.; Shao, Z.-H., Ligand-Controlled Enantioselective [2 + 2] Cycloaddition of Oxabicyclic Alkenes with Terminal Alkynes Using Chiral Iridium Catalysts. *Organic Letters* **2010,** *12* (2), 304-306.
12. Yang, Q.; Yu, L.; Xu, J.; Li, S.; Liu, S.; Chen, H.; Zhou, Y.; Wang, L.; Fan, B.,

Kinetic resolution of C1-substituted oxabenzonorbornadienes by Ir-catalyzed asymmetric [2+2] cycloaddition reactions with arylacetylenes. *Tetrahedron: Asymmetry* **2014,** *25* (13), 957-961.

13. Nishimura, A.; Ohashi, M.; Ogoshi, S., Nickel-Catalyzed Intermolecular [2 + 2] Cycloaddition of Conjugated Enynes with Alkenes. *Journal of the American Chemical Society* **2012,** *134* (38), 15692-15695.

14. Kossler, D.; Cramer, N., Neutral chiral cyclopentadienyl Ru(ii)Cl catalysts enable enantioselective [2+2]-cycloadditions. *Chemical Science* **2017,** *8* (3), 1862-1866.

15. Pagar, V. V.; RajanBabu, T. V., Tandem catalysis for asymmetric coupling of ethylene and enynes to functionalized cyclobutanes. *Science* **2018,** *361* (6397), 68-72.

16. Iwai, T.; Ueno, M.; Okochi, H.; Sawamura, M., Synthesis of Cyclobutene-Fused Eight-Membered Carbocycles through Gold-Catalyzed Intramolecular Enyne [2+2] Cycloaddition. *Advanced Synthesis & Catalysis* **2018,** *360* (4), 670-675.

17. Bai, Y.-B.; Luo, Z.; Wang, Y.; Gao, J.-M.; Zhang, L., Au-Catalyzed Intermolecular [2+2] Cycloadditions between Chloroalkynes and Unactivated Alkenes. *Journal of the American Chemical Society* **2018,** *140* (17), 5860-5865.

18. Poplata, S.; Troster, A.; Zou, Y. Q.; Bach, T., Recent Advances in the Synthesis of Cyclobutanes by Olefin [2+2] Photocycloaddition Reactions. *Chem Rev* **2016,** *116* (17), 9748-815.

19. Ruider, S. A.; Sandmeier, T.; Carreira, E. M., Total Synthesis of (±)-Hippolachnin A. *Angewandte Chemie International Edition* **2015,** *54* (8), 2378-2382.

20. Bradford, C. L.; Fleming, S. A.; Ward, S. C., Regio-controlled ene-yne photochemical [2 + 2] cycloaddition using silicon as a tether. *Tetrahedron Letters* **1995,** *36* (24), 4189-4192.

21. Kokubo, K.; Yamaguchi, H.; Kawamoto, T.; Oshima, T., Substituent Effects on the Stereochemistry in the [2 + 2] Photocycloaddition Reaction of Homobenzoquinone Derivative with Variously Substituted Alkenes and Alkynes. *Journal of the American Chemical Society* **2002,** *124* (30), 8912-8921.

22. Ralph, M. J.; Harrowven, D. C.; Gaulier, S.; Ng, S.; Booker-Milburn, K. I., The Profound Effect of the Ring Size in the Electrocyclic Opening of Cyclobutene-Fused Bicyclic Systems. *Angewandte Chemie International Edition* **2015,** *54* (5), 1527-1531.

23. Hook, B. D. A.; Dohle, W.; Hirst, P. R.; Pickworth, M.; Berry, M. B.; Booker-Milburn, K. I., A Practical Flow Reactor for Continuous Organic Photochemistry. *The Journal of Organic Chemistry* **2005,** *70* (19), 7558-7564.

24. Maturi, M. M.; Bach, T., Enantioselective Catalysis of the Intermolecular [2+2] Photocycloaddition between 2-Pyridones and Acetylenedicarboxylates. *Angewandte Chemie International Edition* **2014,** *53* (29), 7661-7664.

25. Blum, T. R.; Miller, Z. D.; Bates, D. M.; Guzei, I. A.; Yoon, T. P., Enantioselective photochemistry through Lewis acid–catalyzed triplet energy transfer. *Science* **2016,** *354* (6318), 1391-1395.

26. Skubi, K. L.; Kidd, J. B.; Jung, H.; Guzei, I. A.; Baik, M. H.; Yoon, T. P., Enantioselective Excited-State Photoreactions Controlled by a Chiral Hydrogen-Bonding Iridium Sensitizer. *J Am Chem Soc* **2017,** *139* (47), 17186-17192.

27. Lei, T.; Zhou, C.; Huang, M. Y.; Zhao, L. M.; Yang, B.; Ye, C.; Xiao, H.; Meng, Q. Y.; Ramamurthy, V.; Tung, C. H.; Wu, L. Z., General and Efficient Intermolecular [2+2] Photodimerization of Chalcones and Cinnamic Acid Derivatives in Solution through Visible-Light Catalysis. *Angew Chem Int Ed Engl* **2017,** *56* (48), 15407-15410.

28. Zhou, C.; Lei, T.; Wei, X. Z.; Liu, Z.; Chen, B.; Ramamurthy, V.; Tung, C. H.; Wu, L. Z., Chemo- and Regioselective Synthesis of Alkynyl Cyclobutanes by Visible Light Photocatalysis. *Org Lett* **2018,** *20* (21), 6808-6811.

29. Hörmann, F. M.; Chung, T. S.; Rodriguez, E.; Jakob, M.; Bach, T., Evidence for Triplet Sensitization in the Visible-Light-Induced [2+2] Photocycloaddition of Eniminium Ions. *Angewandte Chemie International Edition* **2018,** *57* (3), 827-831.

30. James, M. J.; Schwarz, J. L.; Strieth-Kalthoff, F.; Wibbeling, B.; Glorius, F., Dearomative Cascade Photocatalysis: Divergent Synthesis through Catalyst Selective Energy Transfer. *Journal of the American Chemical Society* **2018,** *140* (28), 8624-8628.

31. Zhu, M.; Zheng, C.; Zhang, X.; You, S. L., Synthesis of Cyclobutane-Fused Angular Tetracyclic Spiroindolines via Visible-Light-Promoted Intramolecular Dearomatization of Indole Derivatives. *J Am Chem Soc* **2019,** *141* (6), 2636-2644.

32. Strieth-Kalthoff, F.; Henkel, C.; Teders, M.; Kahnt, A.; Knolle, W.; Gómez-Suárez, A.; Dirian, K.; Alex, W.; Bergander, K.; Daniliuc, C. G.; Abel, B.; Guldi, D. M.; Glorius, F., Discovery of Unforeseen Energy-Transfer-Based Transformations Using a Combined Screening Approach. *Chem* **2019,** *5* (8), 2183-2194.

33. Lanzi, M.; Santacroce, V.; Balestri, D.; Marchio, L.; Bigi, F.; Maggi, R.; Malacria, M.; Maestri, G., Visible-Light-Promoted Polycyclizations of Dienynes. *Angew Chem Int Ed Engl* **2019,** *58* (20), 6703-6707.

34. Namyslo, J. C.; Kaufmann, D. E., The Application of Cyclobutane Derivatives in Organic Synthesis. *Chemical Reviews* **2003,** *103* (4), 1485-1538.

35. Souris, C.; Luparia, M.; Frébault, F.; Audisio, D.; Farès, C.; Goddard, R.; Maulide, N., An Atom-Economical and Stereoselective Domino Synthesis of Functionalised Dienes. *Chemistry – A European Journal* **2013,** *19* (21), 6566-6570.

36. Adam, W.; Oppenlaender, T.; Zang, G., The 185-nm photochemistry of cyclobutene and bicyclo[1.1.0]butane. *Journal of the American Chemical Society* **1985,** *107* (13), 3921-3924.

37. Clark, K. B.; Leigh, W. J., Cyclobutene photochemistry. Nonstereospecific photochemical ring opening of simple cyclobutenes. *Journal of the American Chemical Society* **1987,** *109* (20), 6086-6092.

38. Ha, S.; Lee, Y.; Kwak, Y.; Mishra, A.; Yu, E.; Ryou, B.; Park, C.-M., Alkyne–Alkene [2 + 2] cycloaddition based on visible light photocatalysis. *Nature Communications* **2020,** *11* (1), 2509.

39. Borkman, R. F.; Kearns, D. R., Triplet-State Energy Transfer in Liquid Solutions. Acetone-Photosensitized cis-trans Isomerization of Pentene-2. *Journal of the American Chemical Society* **1966,** *88* (15), 3467-3475.

40. Grewer, C.; Brauer, H.-D., Mechanism of the Triplet-State Quenching by Molecular Oxygen in Solution. *The Journal of Physical Chemistry* **1994,** *98* (16), 4230-4235.

41. Cao, B.; Wei, Y.; Shi, M., An atmosphere and light tuned highly diastereoselective synthesis of cyclobuta/penta[b]indoles from aniline-tethered alkylidenecyclopropanes with alkynes. *Chem Commun (Camb)* **2018,** *54* (23), 2870-2873.

42. Cao, B.; Wei, Y.; Ye, C.; Wu, L.-Z.; Shi, M., Mechanistic studies on the atmosphere and light tuned synthesis of cyclobuta/penta[b]indoles. *Organic Chemistry Frontiers* **2018,** *5* (12), 1890-1895.

43. Mainetti, E.; Fensterbank, L.; Malacria, M., New Elements in the Reactivity of α-Cyclopropyl Vinyl Radicals. *Synlett* **2002,** *2002* (06), 923-926.

44. Milnes, K. K.; Gottschling, S. E.; Baines, K. M., Determination of the rate constant for ring opening of an alpha-cyclopropylvinyl radical. *Organic & Biomolecular Chemistry* **2004,** *2* (23), 3530-4.

45. Katz, T. J.; Sivavec, T. M., Metal-catalyzed rearrangement of alkene-alkynes and the stereochemistry of metallacyclobutene ring opening. *Journal of the American Chemical Society* **1985,** *107* (3), 737-738.

46. Kinoshita, A.; Mori, M., Ruthenium Catalyzed Enyne Metathesis. *Synlett* **1994,** *1994* (12), 1020-1022.

47. Jung, K.; Kang, E.-H.; Sohn, J.-H.; Choi, T.-L., Highly β-Selective Cyclopolymerization of 1,6-Heptadiynes and Ring-Closing Enyne Metathesis Reaction Using Grubbs Z-Selective Catalyst: Unprecedented Regioselectivity for Ru-Based Catalysts. *Journal of the American Chemical Society* **2016,** *138* (35), 11227-11233.

48. Fürstner, A.; Stelzer, F.; Szillat, H., Platinum-Catalyzed Cycloisomerization Reactions of Enynes. *Journal of the American Chemical Society* **2001,** *123* (48), 11863-11869.

49. Nieto-Oberhuber, C.; López, S.; Muñoz, M. P.; Cárdenas, D. J.; Buñuel, E.; Nevado,

C.; Echavarren, A. M., Divergent Mechanisms for the Skeletal Rearrangement and [2+2] Cycloaddition of Enynes Catalyzed by Gold. *Angewandte Chemie International Edition* **2005,** *44* (38), 6146-6148.

50. Ota, K.; Lee, S. I.; Tang, J.-M.; Takachi, M.; Nakai, H.; Morimoto, T.; Sakurai, H.; Kataoka, K.; Chatani, N., Rh(II)-Catalyzed Skeletal Reorganization of 1,6- and 1,7-Enynes through Electrophilic Activation of Alkynes. *Journal of the American Chemical Society* **2009,** *131* (42), 15203-15211.

51. Nicolaou, K. C.; Bulger, P. G.; Sarlah, D., Metathesis reactions in total synthesis. *Angew Chem Int Ed Engl* **2005,** *44* (29), 4490-527.

52. Kinoshita, A.; Mori, M., Total Synthesis of (−)-Stemoamide Using Ruthenium-Catalyzed Enyne Metathesis Reaction. *The Journal of Organic Chemistry* **1996,** *61* (24), 8356-8357.

53. Layton, M. E.; Morales, C. A.; Shair, M. D., Biomimetic Synthesis of (−)-Longithorone A. *Journal of the American Chemical Society* **2002,** *124* (5), 773-775.

54. Boyer, F.-D.; Hanna, I.; Ricard, L., Formal Synthesis of (±)-Guanacastepene A: A Tandem Ring-Closing Metathesis Approach. *Organic Letters* **2004,** *6* (11), 1817-1820.

55. Allard, S.; Forster, M.; Souharce, B.; Thiem, H.; Scherf, U., Organic Semiconductors for Solution-Processable Field-Effect Transistors (OFETs). *Angewandte Chemie International Edition* **2008,** *47* (22), 4070-4098.

56. Cao, D.; Liu, Z.; Verwilst, P.; Koo, S.; Jangjili, P.; Kim, J. S.; Lin, W., Coumarin-Based Small-Molecule Fluorescent Chemosensors. *Chemical Reviews* **2019,** *119* (18), 10403-10519.

57. Shanmugaraju, S.; Mukherjee, P. S., π-Electron rich small molecule sensors for the recognition of nitroaromatics. *Chemical Communications* **2015,** *51* (89), 16014-16032.

58. Tasior, M.; Kim, D.; Singha, S.; Krzeszewski, M.; Ahn, K. H.; Gryko, D. T., π-Expanded coumarins: synthesis, optical properties and applications. *Journal of Materials Chemistry C* **2015,** *3* (7), 1421-1446.

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